PB85-126035

Air Quality Criteria for Ozone and Other Photochemical Oxidants
External Review Draft. Volume 1

(U.S.) Environmental Protection Agency
Research Triangle Park, NC

Jul 84

U.S. Department of Commerce
National Technical Information Service
NTIS

United States
Environmental Protection
Agency

Environmental Criteria and
Assessment Office
Research Triangle Park NC 27711

EPA-600/8-84-020A
July 1984
External Review Draft

PB85-126035

Research and Development

EPA

Air Quality Criteria for Ozone and Other Photochemical Oxidants

Review Draft

(Do Not
Cite or Quote)

Volume I of V

NOTICE

This document is a preliminary draft. It has not been formally released by EPA and should not at this stage be construed to represent Agency policy. It is being circulated for comment on its technical accuracy and policy implications.

REPRODUCED BY
NATIONAL TECHNICAL
INFORMATION SERVICE
U.S. DEPARTMENT OF COMMERCE
SPRINGFIELD, VA. 22161

TECHNICAL REPORT DATA

(Please read Instructions on the reverse before completing)

1. REPORT NO. EPA-600/8-84-020A -1	2.	3. RECIPIENT'S ACCESSION NO. PB85 126035
4. TITLE AND SUBTITLE Air Quality Criteria for Ozone and Other Photochemical Oxidants. Volume I of V.		5. REPORT DATE July 1984 6. PERFORMING ORGANIZATION CODE
7. AUTHOR(S) See list of authors, contributors, and reviewers		8. PERFORMING ORGANIZATION REPORT NO.
9. PERFORMING ORGANIZATION NAME AND ADDRESS U.S. Environmental Protection Agency Office of Health and Environmental Assessment Environmental Criteria and Assessment Office (MD-52) Research Triangle Park, NC 27711		10. PROGRAM ELEMENT NO. 11. CONTRACT/GRANT NO.
12. SPONSORING AGENCY NAME AND ADDRESS U.S. Environmental Protection Agency Office of Research and Development (RD-689) 401 M Street, S.W. Washington, D.C. 20460		13. TYPE OF REPORT AND PERIOD COVERED External Review Draft 14. SPONSORING AGENCY CODE EPA/600/22

15. SUPPLEMENTARY NOTES

16. ABSTRACT

Scientific information is presented and evaluated relative to the health and welfare effects associated with exposure to ozone and other photochemical oxidants. Though not intended as a complete, detailed literature review, the document covers pertinent literature through 1983 and early 1984.

Data on health and welfare effects are emphasized, but additional information is provided for understanding the nature of the oxidant pollution problem and for evaluating the reliability of effects data as well as their relevance to potential exposures to ozone and other photochemical oxidants at concentrations occurring in ambient air. Separate chapters are presented on the following exposure-related topics pertaining to ozone and other photochemical oxidants: properties, chemistry, and measurement; concentrations typically found in ambient air; formation and transport once formed; and nature, source, measurement, and concentrations of precursors.

The specific areas addressed by chapters on health and welfare effects are: the toxicological appraisal of effects of ozone and other oxidants; effects observed in controlled, human exposures; effects observed in field and epidemiological studies; effects on vegetation seen in field and controlled exposures; effects on natural and agroecosystems; and effects on nonbiological materials observed in field and chamber studies.

17. KEY WORDS AND DOCUMENT ANALYSIS

a. DESCRIPTORS	b. IDENTIFIERS/OPEN ENDED TERMS	c. COSATI Field/Group

18. DISTRIBUTION STATEMENT Release to Public	19. SECURITY CLASS *(This Report)* Unclassified	21. NO. OF PAGES 219
	20. SECURITY CLASS *(This page)* Unclassified	22. PRICE

EPA Form 2220-1 (Rev. 4-77) PREVIOUS EDITION IS OBSOLETE

Draft
Do Not Quote or Cite

EPA-600/8-84-020A - 1
July 1984
External Review Draft

Air Quality Criteria for Ozone and Other Photochemical Oxidants

Volume I of V

NOTICE

This document is a preliminary draft. It has not been formally released by EPA and should not at this stage be construed to represent Agency policy. It is being circulated for comment on its technical accuracy and policy implications.

Environmental Criteria and Assessment Office
Office of Health and Environmental Assessment
Office of Research and Development
U.S. Environmental Protection Agency
Research Triangle Park, N.C. 27711

i-a

NOTICE

Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

ABSTRACT

Scientific information is presented and evaluated relative to the health and welfare effects associated with exposure to ozone and other photochemical oxidants. Although it is not intended as a complete and detailed literature review, the document covers pertinent literature through 1983 and early 1984.

Data on health and welfare effects are emphasized, but additional information is provided for understanding the nature of the oxidant pollution problem and for evaluating the reliability of effects data as well as their relevance to potential exposures to ozone and other oxidants at concentrations occurring in ambient air. Separate chapters are presented on the following exposure-related topics: nature, source, measurement, and concentrations of precursors to ozone and other photochemical oxidants; the formation of ozone and other photochemical oxidants and their transport once formed; the properties, chemistry, and measurement of ozone and other photochemical oxidants; and the concentrations of ozone and other photochemical oxidants that are typically found in ambient air.

The specific areas addressed by chapters on health and welfare effects are the toxicological appraisal of effects of ozone and other oxidants; effects observed in controlled human exposures; effects observed in field and epidemiological studies; effects on vegetation seen in field and controlled exposures; effects on natural and agroecosystems; and effects on nonbiological materials observed in field and chamber studies.

CONTENTS

Page

VOLUME I
Chapter 1. Summary and Conclusions 1-1

VOLUME II
Chapter 2. Introduction 2-1
Chapter 3. Precursors to Ozone and Other Photochemical Oxidants 3-1
Chapter 4. Chemical and Physical Processes in the Formation and Occurrence of Ozone and Other Photochemical Oxidants 4-1
Chapter 5. Properties, Chemistry, and Measurement of Ozone and Other Photochemical Oxidants 5-1
Chapter 6. Concentrations of Ozone and Other Photochemical Oxidants in Ambient Air 6-2

VOLUME III
Chapter 7. Effects of Ozone and Other Photochemical Oxidants on Vegetation 7-1
Chapter 8. Effects of Ozone and Other Photochemical Oxidants on Natural and Agroecosystems 8-1
Chapter 9. Effects of Ozone and Other Photochemical Oxidants on Nonbiological Materials 9-1

VOLUME IV
Chapter 10. Toxicological Effects of Ozone and Other Photochemical Oxidants 10-1

VOLUME V
Chapter 11. Controlled Human Studies of the Effects of Ozone and Other Photochemical Oxidants 11-1
Chapter 12. Field and Epidemiological Studies of the Effects of Ozone and Other Photochemical Oxidants 12-1
Chapter 13. Evaluation of Integrated Health Effects Data for Ozone and Other Photochemical Oxidants 13-1

TABLE OF CONTENTS

Page

LIST OF TABLES ix
LIST OF FIGURES x
AUTHORS AND CONTRIBUTORS xii
LIST OF ABBREVIATIONS AND SYMBOLS xv

1. SUMMARY AND CONCLUSIONS 1-1
  1.1 INTRODUCTION 1-1
  1.2 PRECURSORS TO OZONE AND OTHER PHOTOCHEMICAL OXIDANTS 1-2
    1.2.1 Nature of Precursors 1-2
    1.2.2 Measurement of Precursors 1-3
    1.2.3 Sources and Emissions of Precursors 1-6
    1.2.4 Ambient Air Concentrations of Precursors 1-8
  1.3 CHEMICAL AND PHYSICAL PROCESSES IN THE FORMATION AND OCCURRENCE OF OZONE AND OTHER PHOTOCHEMICAL OXIDANTS 1-12
    1.3.1 Chemical Processes 1-12
    1.3.2 Physical Processes 1-14
  1.4 PROPERTIES, CHEMISTRY, AND MEASUREMENT OF OZONE AND OTHER PHOTOCHEMICAL OXIDANTS 1-15
    1.4.1 Properties 1-15
    1.4.2 Reactions of Ozone and Other Oxidants in Ambient Air 1-16
    1.4.3 Reactions of Ozone and Peroxyacetyl Nitrate in Aqueous (Biological) Systems 1-17
    1.4.4 Sampling and Measurement of Ozone and Other Photochemical Oxidants 1-18
      1.4.4.1 Quality Assurance and Sampling 1-19
      1.4.4.2 Measurement Methods for Total Oxidants and Ozone 1-20
      1.4.4.3 Calibration Methods 1-23
      1.4.4.4 Relationship of Total Oxidants and Ozone Measurements 1-25
      1.4.4.5 Methods for Sampling and Analysis of Peroxyacetyl Nitrate and Its Homologues 1-27
      1.4.4.6 Methods for Sampling and Analysis of Hydrogen Peroxide 1-32
  1.5 CONCENTRATIONS OF OZONE AND OTHER PHOTOCHEMICAL OXIDANTS IN AMBIENT AIR 1-36
    1.5.1 Ozone Concentrations in Urban Areas 1-37
    1.5.2 Trends in Urban and Nationwide Ozone Concentrations 1-40
    1.5.3 Ozone Concentrations in Nonurban Areas 1-42
    1.5.4 Patterns in Ozone Concentrations 1-43
    1.5.5 Concentrations and Patterns of Other Photochemical Oxidants 1-45
      1.5.5.1 Concentrations 1-45
      1.5.5.2 Patterns 1-47

TABLE OF CONTENTS
(continued)

Page

1.5.6 Relationship Between Ozone and Other Photochemical Oxidants 1-48
1.6 EFFECTS OF OZONE AND PEROXYACETYL NITRATE ON VEGETATION .. 1-51
1.6.1 Effects of Ozone on Vegetation 1-51
1.6.1.1 Introduction 1-51
1.6.1.2 Limiting Values of Plant Response 1-52
1.6.1.3 Methods for Determining Ozone Yield Losses 1-55
1.6.1.4 Estimates of Yield Loss 1-56
1.6.1.5 Effects on Crop Quality 1-64
1.6.1.6 Yield Loss from Ambient Exposures 1-64
1.6.1.7 Statistics Used to Characterize Ozone Exposures 1-64
1.6.1.8 Relation Between Yield Loss and Foliar Injury 1-66
1.6.1.9 Physiological Basis of Yield Reductions 1-66
1.6.1.10 Factors Affecting Plant Response to Ozone 1-67
1.6.1.11 Economic Assessment of Ozone Effects ... 1-69
1.6.2 Effects of Peroxyacetyl Nitrate on Vegetation 1-71
1.6.2.1 Introduction 1-71
1.6.2.2 Factors Affecting Plant Response to PAN 1-71
1.6.2.3 Limiting Values of Plant Response 1-71
1.6.2.4 Effects of PAN on Plant Yield 1-72
1.7 EFFECTS OF OZONE AND OTHER PHOTOCHEMICAL OXIDANTS ON NATURAL ECOSYSTEMS 1-72
1.7.1 Introduction 1-72
1.7.2 Oxidant-Induced Effects on a Western Coniferous Forest Ecosystem 1-74
1.7.3 Effects of Ozone on Other Ecosystems 1-77
1.7.4 Effects on Interrelated Ecosystems 1-80
1.7.4.1 Aquatic Ecosystems 1-80
1.7.4.2 Agricultural Ecosystems 1-81
1.7.5 Ecosystem Responses to Stress 1-81
1.8 EFFECTS OF OZONE AND OTHER PHOTOCHEMICAL OXIDANTS ON NONBIOLOGICAL MATERIALS 1-83
1.8.1 Introduction 1-83
1.8.2 Effects and Damage Functions 1-84
1.8.2.1 Elastomers 1-84
1.8.2.2 Textile Fibers and Dyes 1-85
1.8.2.3 Paints 1-87
1.8.3 Economic Assessment of Effects of Ozone on Materials 1-87
1.9 INTRODUCTION TO HEALTH EFFECTS 1-89
1.9.1 Organization of Health Effects Information 1-89
1.9.2 Literature Coverage and Selection 1-92

TABLE OF CONTENTS
(continued)

Page

1.10 TOXICOLOGIC EFFECTS OF OZONE AND OTHER PHOTOCHEMICAL OXIDANTS 1-93
  1.10.1 Introduction 1-93
  1.10.2 Respiratory Transport and Absorption of Ozone 1-94
  1.10.3 Effects of Ozone on the Respiratory Tract 1-96
    1.10.3.1 Morphological Effects 1-96
    1.10.3.2 Pulmonary Function 1-99
    1.10.3.3 Biochemical Effects of Ozone in the Lung of Experimental Animals 1-105
    1.10.3.4 Effects of Ozone in Altering Host Defense Against Microbes 1-110
    1.10.3.5 Tolerance 1-115
  1.10.4 Extrapulmonary Effects of Ozone 1-118
    1.10.4.1 Central Nervous System and Behavioral Effects 1-118
    1.10.4.2 Cardiovascular Effects 1-119
    1.10.4.3 Hematological and Serum Chemistry Effects 1-119
    1.10.4.4 Cytogenetic and Teratogenetic Effects 1-121
    1.10.4.5 Other Extrapulmonary Effects 1-122
  1.10.5 Effects of Other Photochemical Oxidants 1-123
1.11 EFFECTS OF OZONE AND OTHER PHOTOCHEMICAL OXIDANTS IN CONTROLLED EXPOSURES 1-127
  1.11.1 Pulmonary Function Effects in Controlled Human Studies: Mechanical Function of the Lung 1-127
    1.11.1.1 General Population 1-127
    1.11.1.2 Subjects with Preexisting Disease 1-136
    1.11.1.3 Intersubject Variability 1-137
    1.11.1.4 Attenuation with Repeated Exposures 1-137
  1.11.2 Other Effects of Ozone in Controlled Human Exposures 1-138
  1.11.3 Effects of Peroxyacetyl Nitrate and Mixtures in Controlled Human Exposures 1-139
1.12 FIELD AND EPIDEMIOLOGICAL STUDIES OF THE EFFECTS OF OZONE AND OXIDANTS 1-139
  1.12.1 Introduction 1-139
  1.12.2 Field and Epidemiological Studies of Effects of Effects of Acute Exposure 1-140
  1.12.3 Epidemiological studies of Effects of Chronic Exposure 1-143
1.13 SUMMARY OF THE EVALUATION OF INTEGRATED HEALTH EFFECTS DATA 1-144
  1.13.1 Health Effects in the General Human Population 1-144
  1.13.2 Health Effects in Potentially Susceptible Individuals 1-148
  1.13.3 Extrapolation of Effects Observed in Animals to Human Populations 1-149

TABLE OF CONTENTS
(continued)

Page

1.13.4 Health Effects of Other Photochemical Oxidants and Pollutant Mixtures 1-150

1.13.5 Identification of Potentially At-Risk Populations or Subpopulations 1-150

1.14 REFERENCES 1-153

LIST OF TABLES

Table		Page
1-1	Hydrocarbon (HC) composition typically measured in urban areas (from sample collected in Milwaukee, 1981)	1-10
1-2	Summary of ozone monitoring techniques	1-22
1-3	Ozone calibration techniques	1-24
1-4	Summary of parameters used in determination of PAN by GC-ECD	1-29
1-5	Infrared absorptivities of peroxyacetyl nitrate	1-30
1-6	Measurement methods for hydrogen peroxide	1-34
1-7	Second-highest 1-hr ozone concentrations in 1982 in Standard Metropolitan Statistical Areas with populations >1 million, given by census divisions and regions	1-38
1-8	Ozone concentrations for short-term exposures that produce 5 or 20 percent injury to vegetation grown under sensitive conditions	1-53
1-9	Seasonal 7-hour ozone concentrations (ppm) at which yield losses of 10 percent or 30 percent are predicted from exposure-response models	1-60
1-10	Ozone concentrations at which significant yield losses have been noted for a variety of plant species exposed to O_3 under various experimental conditions	1-62
1-11	Injury thresholds for 2-hour exposures to ozone	1-79
1-12	Morphological effects of ozone in experimental animals	1-101
1-13	Effects on pulmonary function of short-term exposures to ozone	1-104
1-14	Effects on pulmonary function of long-term exposures to ozone	1-107
1-15	Biochemical changes in experimental animals exposed to ozone ..	1-112
1-16	Effects of ozone on host defense mechanisms in experimental animals	1-117
1-17	Extrapulmonary effects of ozone in experimental animals	1-125
1-18	Summary table: Results of controlled human exposures to ozone	1-128
1-19	Estimated values of oxygen consumption and minute ventilation associated with representative types of exercise	1-133
1-20	Summary table: Acute effects of ozone and other photochemical oxidants in population studies	1-141

LIST OF FIGURES

Figure — Page

1-1 National trend in estimated emissions of volatile organic compounds, 1970 through 1982 1-7
1-2 National trend in estimated emissions of nitrogen oxides, 1970 through 1982 1-9
1-3 Collective distributions of the three highest 1-hour ozone concentrations for 3 years (1979, 1980, and 1981) at valid sites (906 station-years) 1-41
1-4 Relationship between O_3 concentration, exposure duration, and a reduction in plant growth or yield (see Table 7-18; also U.S. EPA, 1978) 1-54
1-5 Examples of effects of O_3 exposure on yield of various plants. O_3 concentration (ppm) is expressed as 7-hr seasonal mean. Soybean (A) data from Kress and Miller (1983); peanut (B) data from Heagle et al. (1983) and Heck et al. (1982); corn (C) and wheat (D) data from Heagle and Heck (1980) and Heck et al. (1982) 1-57
1-6 Relative O_3-induced yield reduction of selected crops as predicted by the Weibull model (Heck et al., 1983) 1-58
1-7 Summation of abiotic and biotic agents involved in diseases of trees, given by types of diseases and functional parts of the tree. Decline diseases are caused by a combination of biotic and abiotic agents 1-73
1-8 Conceptual sequence of levels showing continuum of plant responses 1-82
1-9 Summary of morphological effects in experimental animals exposed to ozone 1-100
1-10 Summary of effects of short-term ozone exposures on pulmonary function in experimental animals 1-103
1-11 Summary of effects of long-term ozone exposures on pulmonary function in experimental animals 1-106
1-12 Summary of biochemical changes in experimental animals exposed to ozone 1-111
1-13 Summary of effects of ozone on host defense mechanisms in experimental animals 1-116
1-14 Summary of extrapulmonary effects of ozone in experimental animals 1-124
1-15 Group mean decrements in 1-sec forced expiratory volume during 2-hr ozone exposures with different levels of intermittent exercise: light ($\dot{V}_E < 25$ L/min); moderate ($\dot{V}_E = 26$-43 L/min); heavy ($\dot{V}_E = 44$-63 L/min); and very heavy ($\dot{V}_E \geq 64$ L/min) 1-135

Project Team: Air Quality Criteria for Ozone and Other Photochemical Oxidants

Ms. Beverly E. Tilton, Project Manager
and Coordinator for Chapters 1 through 6
Environmental Criteria and
Assessment Office
MD-52
U.S. Environmental Protection Agency
Research Triangle Park, NC 27711

Dr. J. H. B. Garner
Coordinator for Chapters 8 and 9;
Co-coordinator for Chapter 7
Environmental Criteria and
Assessment Office
MD-52
U.S. Environmental Protection Agency
Research Triangle Park, NC 27711

Mr. Thomas B. McMullen
Assistant Coordinator for Chapters 3 and 4
Environmental Criteria and
Assessment Office
MD-52
U.S. Environmental Protection Agency
Research Triangle Park, NC 27711

Mr. James A. Raub
Coordinator for Chapters 10 through 13
Environmental Criteria and
Assessment Office
MD-52
U.S. Environmental Protection Agency
Research Triangle Park, NC 27711

Dr. David T. Tingey
Coordinator for Chapter 7
Environmental Research Laboratory
U.S. Environmental Protection Agency
200 SW 35th Street
Corvallis, OR 97330

AUTHORS AND CONTRIBUTORS

Chapter 1. Summary and Conclusions

Principal Authors

Dr. Donald E. Gardner
Northrop Services, Inc.
Environmental Sciences
P. O. Box 12313
Research Triangle Park, NC 27709

Dr. J. H. B. Garner
Environmental Criteria and Assessment Office
MD-52
U.S. Environmental Protection Agency
Research Triangle Park, NC 27711

Dr. Judith A. Graham
Health Effects Research Laboratory
MD-82
U.S. Environmental Protection Agency
Research Triangle Park, NC 27711

Dr. Jimmie A. Hodgeson
Professor, Department of Chemistry
407 Choppin Hall
Louisiana State University
Baton Rouge, LA 70803

*Dr. Thomas J. Kulle
Department of Medicine
School of Medicine
29 South Green Street, GSB-414
University of Maryland
Baltimore, MD 21201

Mr. James A. Raub
Environmental Criteria and Assessment Office
MD-52
U.S. Environmental Protection Agency
Research Triangle Park, NC 27711

Ms. Beverly E. Tilton
Environmental Criteria and Assessment Office
MD-52
U.S. Environmental Protection Agency
Research Triangle Park, NC 27711

Dr. David T. Tingey
Environmental Research Laboratory
200 SW 35th Street
Corvallis, OR 97330

Contributing Authors

*Dr. Robert Frank
Department of Environmental Health Sciences
Johns Hopkins School of Hygiene and Public Health
615 N. Wolfe Street
Baltimore, MD 21205

*Dr. Milan J. Hazucha
School of Medicine
Center for Environmental Health and Medical Sciences
University of North Carolina
Chapel Hill, NC 27514

Mr. Michael W. Holdren
Battelle, Columbus Laboratories
505 King Avenue
Columbus, OH 43201

Dr. Donald H. Horstman
Health Effects Research Laboratory
MD-58
U.S. Environmental Protection Agency
Research Triangle Park, NC 27711

Mr. James M. Kawecki
TRC Environmental Consultants
701 West Broad Street
Suite 401
Falls Church, VA 22046

Dr. Jan G. Laarman
Department of Forestry
North Carolina State University
Raleigh, NC 27607

Dr. Michael D. Lebowitz
Department of Internal Medicine
College of Medicine
University of Arizona
Tucson, AZ 85724

Mr. Thomas B. McMullen
Environmental Criteria and Assessment Office
MD-52
U.S. Environmental Protection Agency
Research Triangle Park, NC 27711

Dr. Daniel B. Menzel
Laboratory of Environmental Toxicology and Pharmacology
Duke University Medical Center
P. O. Box 3813
Durham, NC 27710

Contributing Authors (continued)

Dr. Harold G. Richter
Office of Air Quality Planning and Standards
Monitoring and Data Analysis Division
MD-14
U.S. Environmental Protection Agency
Research Triangle Park, NC 27711

Dr. Halvor Westberg
Director, Laboratory for Atmospheric Research,
and Professor, Civil and Environmental Engineering
Washington State University
Pullman, WA 99164-2730

Dr. Arthur M. Winer
Assistant Director
Statewide Air Pollution Research Center
University of California
Riverside, CA 92521

---

*These authors also reviewed portions of Chapter 1 at the request of the U.S. Environmental Protection Agency. The evaluations and conclusions contained herein, however, are not necessarily those of the reviewers.

LIST OF ABBREVIATIONS

ACh	acetylcholine
AFR	air:fuel ratio
AM	alveolar macrophage
ANOVA	analysis of variance
AOD	airway obstructive disease
APHA	American Public Health Association
~	approximately
aq	aqueous
ASL	above sea level
atm	atmosphere
ATPS	ATPS condition (ambient temperature and pressure, saturated with water vapor)
avg	average
b.p.	boiling point
BTPS	BTPS conditions (body temperature, barometric pressure, and saturated with water vapor)
bz	benzene
C	carbon
°C	degrees Celsius
CA	chromotropic acid
CAMP	Continuous Air Monitoring Program
CARB	California Air Resources Board
cc	cubic centimeter
CC	closing capacity
C_{dyn}	dynamic lung compliance
CE	continuous exercise
CHEM	gas phase chemiluminescence
CH_4	methane
CHESS	Community Health Environmental Surveillance System
C_L	lung compliance
C_{Lst}	static lung compliance
cm	centimeter

LIST OF ABBREVIATIONS (continued)

CNS	central nervous system
CO	carbon monoxide
CO_2	carbon dioxide
COHb	carboxyhemoglobin
COLD	chronic obstructive lung disease
concn	concentration
COPD	chronic obstructive pulmonary disease
CV	closing volume
DBH	tree diameter at breast height
D_L	diffusing capacity of the lungs
D_{LCO}	carbon monoxide diffusion capacity of the lungs
DNPH	2,4-dinitrophenylhydrazine
DOT	Department of Transportation
E	elastance
ECD	electron-capture detector
ECG, EKG	electrocardiogram
EEG	electroencephalogram
EKMA	Empirical Kinetic Modeling Approach
$E_0^\cdot$	normal electrode potential
EPA	U.S. Environmental Protection Agency
ERV	expiratory reserve volume
FEF_{max}	maximal forced expiratory flow achieved during an FVC
FEF	forced expiratory flow
$FEF_{200-1200}$	mean forced expiratory flow between 200 ml and 1200 ml of the FVC [formerly called the maximum expiratory flow rate (MEFR)]
$FEF_{25-75\%}$	mean forced expiratory flow during the middle half of the FVC [formerly called the maximum mid-expiratory flow rate (MMFR)]
$FEF_{75\%}$	instantaneous forced expiratory flow after 75% of the FVC has been exhaled

LIST OF ABBREVIATIONS (continued)

FEV	forced expiratory volume
FEV_1	forced expiratory volume in 1 sec
FEV_t/FVC	a ratio of timed forced expiratory volume (FEV_t) to forced vital capacity (FVC)
FID	flame ionization detector
FIVC	forced inspiratory vital capacity
f_R	respiratory frequency
FRC	functional residual capacity
FRM	Federal Reference Method
ft	foot
FTIR	Fourier-transform infrared
FVC	forced vital capacity
G	conductance
g	grams(s)
G-6-PD	glucose-6-phosphate dehydrogenase
Gaw	airway conductance
GC	gas chromatography
g/mi	grams per mile
GPT	gas-phase titration
GS-CHEM	gas-solid chemiluminescence
GSH	glutathione
Hb	hemoglobin
HC	hydrocarbons
HCN	hydrogen cyanide
HCOOH	formic acid
Hct	hematocrit
HFET	Highway Fuel Economy Driving Schedule
Hg	mercury
HO·	hydroxy radical
HO_2	hydroperoxy
HONO	nitrous acid
$HONO_2$	nitric acid

LIST OF ABBREVIATIONS (continued)

HPLC	high-pressure liquid chromatograpy; also,
HPPA	3-(p-hydroxyphenyl)propionic acid
hr	hour(s)
hr/day	hours per day
HRP	Horseradish peroxidase
H_2O	water
H_2O_2	hydrogen peroxide
H_2SO_4	sulfuric acid
hv	photon
IC	inspiratory capacity
IE	intermittent exercise
in	inch(es)
IR	infrared
IRV	inspiratory reserve volume
IVC	inspiratory vital capacity
k	constant
kg	kilogram
kgm/min	kilogram-meter/min
KI	potassium iodide
km	kilometer
LDH	lactate deyhydrogenase
LD_{50}	lethal dose (50 percent)
LM	light microscopy
L/min	liters/min
ln	natural logarithm (base e)
L/s	liters/sec
LST	local standard time
M	molar
m	meter(s)
MAST	KI-coulometric (Mast meter)
max $\dot{V}_E$	maximum ventilation
max $\dot{V}O_2$	maximal aerobic capacity

LIST OF ABBREVIATIONS (continued)

mb	millibar(s)
MBC	maximum breathing capacity
MBTH	3-methyl-2-benzothiazolinone hydrazone
MEFR	maximum expiratory flow rate
MEFV	maximum expiratory flow-volume curve
MetHb	methemoglobin
mg	milligram(s)
mg/m^3	milligrams per cubic meter
MGE	modified graphite electrode
min	minute(s)
ml	milliliter(s)
mm	millimeter(s)
mM	millimolar
MMAD	mass median aerodynamic diameter
MMC	mean meridional circulation
MMFR or MMEF	maximum mid-expiratory flow rate
m.p.	melting point
mph	miles per hour
MS	mass spectrometry
MSL	mean sea level
MT	metric tons
MTBE	methyl tertiary butyl ether
MVV	maximum voluntary ventilation
NA	not available
NAAQS	National Ambient Air Quality Standard
NADB	National Aerometric Data Bank
NAMS	National Aerometric Monitoring Stations
NAPBN	National Air Pollution Background Network
NAS	National Academy of Sciences
NBS	National Bureau of Standards
NBKI	neutral buffered potassium iodide
NECRMP	Northeast Corridor Regional Modeling Project

LIST OF ABBREVIATIONS (continued)

NEDS	National Emissions Data System
NEROS	Northeast Regional Oxidant Study
NH_3	ammonia
$(NH_4)_2SO_4$	ammonium sulfate
NH_4NO_3	ammonium nitrate
NF	National Forest
nm	nanometer
NMHC	nonmethane hydrocarbons
NMOC	nonmethane organic compounds
NO	nitric oxide
NO_2	nitrogen dioxide
NO_3	nitrogen trioxide
NO_x	nitrogen oxides
ΔN_2, dN_2	nitrogen washout
NR	natural rubber
NYCC	New York City Driving Schedule
O_2	oxygen
O_2^-	oxygen radical
O_3	ozone
$P(A-a)O_2$	alveolar-arterial oxygen pressure difference
PABA	para-aminobenzoic acid
P_ACO_2	alveolar partial pressure of carbon dioxide
$PaCO_2$	arterial partial pressure of carbon dioxide
PAN	peroxyacetyl nitrate
P_AO_2	alveolar partial pressure of oxygen
PaO_2	arterial partial pressure of oxygen
PBZN	peroxybenzoyl nitrate
PEF	peak expiratory flow
PEFV	partial expiratory flow-volume curve
PG	prostaglandin
pH	reciprocal of H ion concentration
pH_a	arterial pH

LIST OF ABBREVIATIONS (continued)

P_L	transpulmonary pressure
PMN	polymorphonuclear leukocyte
PNA	peroxynitric acid
PPN	peroxypropionyl nitrate
ppb	parts per billion
ppm	parts per million
ppt	parts per trillion
PSD	prevention of Significant Deterioration
psig	pounds per square inch gauge
P_{st}	static transpulmonary pressure
PST	Pacific Standard Time
PUFA	polyunsaturated fatty acid
R	resistance to flow
RAPS	Regional Air Pollution Study
Raw	airway resistance
RBC	red blood cell
R_{coll}	collateral resistance
rh	relative humidity
R_L	total pulmonary resistance
RQ, R	respiratory quotient
R_t	total respiratory resistance
R_{ti}	tissue resistance
RTI	Research Triangle Institute
RV	residual volume
S.D.	standard deviation
SaO_2	arterial oxygen saturation
SAROAD	Storage and Retrieval of Aerometric Data
SBNT	single-breath nitrogen test
SBR	styrene-butadiene rubber
SCAB	South Coast Air Basin
SCE	sister chromatid exchange
Se	selenium

LIST OF ABBREVIATIONS (continued)

sec	second(s)
SEM	scanning electron microscopy
SGaw	specific airway conductance
SH	sulfhydryls
SLAMS	State and Local Air Monitoring Stations
SMSA	Standard Metropolitan Statistical Area
SOD	superoxide dismutase
SO_2	sulfur dioxide
SO_4	sulfate
SPF	specific pathogen-free
SRaw	specific airway resistance
SRM	standard Reference Material
SSET	small-scale eddy transport
STA	seasonal tropopause adjustment
STP	standard temperature and pressure
STPD	STPD conditions (standard temperature and pressure, dry)
SURE	Sulfate Regional Experiment Sites
TEL	tetraethyl lead
TEM	transmission electron microscopy
Tenax GC	adsorbent used in NMOC analysis
TF	tropopause-folding events
tg/yr	teragrams per year
TGV	thoracic gas volume
THC	total hydrocarbons
TLC	total lung capacity
TML	tetramethyl lead
TNMHC	total nonmethane hydrocarbons
TV	tidal volume
TWC	three-way catalyst
UV	ultraviolet photometry
$\mu g/m^3$	microgram per cubic meter

LIST OF ABBREVIATIONS (continued)

μM	micromolar
U	uranium
UHAC	uranium hydroxamic acid chelates
U.S.	United States
UV	ultraviolet
V	vanadium
$\dot{V}_A$	alveolar ventilation
$\dot{V}_A/\dot{Q}$	ventilation/perfusion ratio
VC	vital capacity
$\dot{V}CO_2$	carbon dioxide production
V_D	physiological dead space
$\dot{V}_D$	dead-space ventilation
$V_{D\ anat}$	anatomical dead space
$\dot{V}_E$	minute ventilation; expired volume per minute
$\dot{V}_I$	inspired volume per minute
V_L	lung volume
$\dot{V}_{max}$	maximum expiratory flow
$\dot{V}O_2$	oxygen uptake
$\dot{V}O_2$, $\dot{Q}O_2$	oxygen consumption
v/v	volume - volume
VHAC	vanadium hydroxamic acid chelates
VOC	volatile organic compounds
vol %	volume percent
w/w	weight - weight
WCOT	wall-coated open tubular (column)
XAD-2	absorbent used in NMOC analysis
XO	xylenol orange
yr	year(s)
λ	wavelength

1. SUMMARY AND CONCLUSIONS

1.1 INTRODUCTION

This document consolidates and assesses knowledge regarding the origin and distribution of ozone and other photochemical oxidants and the effects of these pollutants on humans, experimental animals, vegetation, terrestrial ecosystems, and nonbiological materials. Because the indirect contributions of the photochemical oxidants to visibility degradation, climatic changes, and acidic deposition can not at present be quantified, these atmospheric effects and phenomena are not addressed in this document. They have been fully addressed, however, in other, recent air quality criteria documents (U.S. Environmental Protection Agency, 1982a,b).

While a number of photochemical oxidants have been observed in or postulated to occur in ambient air, only data on ozone, peroxyacyl nitrates, and hydrogen peroxide are examined in this document. Coverage has been limited to these three oxidants on the basis of available information on effects and ambient air concentrations. Of these oxidants, only ozone and peroxyacetyl nitrate have been studied at concentrations having relevance for potential exposures of human populations or of vegetation, ecosystems, or nonbiological materials. Although by definition a photochemical oxidant, nitrogen dioxide is not included among the oxidants discussed in this document. A separate criteria document is issued for oxides of nitrogen, as specified by the Clean Air Act. The second criteria document prepared by the U.S. Environmental Protection Agency (EPA) on the oxides of nitrogen was published in 1982 (U.S. Environmental Protection Agency, 1982a).

This document presents a review and evaluation of literature published through 1983, and in some cases, through early 1984. The document is not intended as a complete literature review, however; but is intended, rather, to present current data of probable consequence for the derivation of national ambient air quality standards for protecting public health and welfare.

In the early chapters of this document, an overview is presented of the nature, origins, and distribution in ambient air of those organic and inorganic compounds that serve as precursors to ozone and other photochemical oxidants. The currently available measurement techniques for these precursors are briefly evaluated, inasmuch as the assessment of the occurrence of the precursors depends upon their accurate measurement. Similarly, an overview is presented of the chemical and physical processes in the atmosphere by which precursors give rise to the production of ozone and other photochemical oxidants. In subsequent chapters, the properties and generic reactions responsible for the effects ascribed to ozone and other photochemical oxidants are presented as background for understanding the detailed information presented in the chapters on health and welfare effects. Likewise, techniques for the measurement of ozone, total oxidants, and individual oxidant species other than ozone are evaluated, since the significance of aerometric and exposure data on these pollutants is dependent upon the accuracy and specificity of the analytical techniques used. Typical concentrations of the respective oxidants are presented to permit assessment of potential exposures of human populations and other receptors.

Remaining chapters of the document contain the actual air quality criteria; that is, quantitative and qualitative information that describes the nature of the health and welfare effects attributable to ozone and other photochemical oxidants and the concentrations at which these pollutants are thought to produce the observed effects.

The legislative basis for the development and issuance of air quality criteria and related information is found in Sections 108 and 109 of the Clean Air Act as amended in 1977 (U.S. Congress, 1977).

1.2 PRECURSORS TO OZONE AND OTHER PHOTOCHEMICAL OXIDANTS

1.2.1 Nature of Precursors

Photochemical oxidants are products of atmospheric reactions involving volatile organic compounds (VOC), oxides of nitrogen (NO_x), hydroxyl radicals, oxygen, and sunlight. They are almost exclusively secondary pollutants, formed in the atmosphere from their precursors by processes that are a complex function of precursor emissions and meteorological factors.

Although vapor-phase hydrocarbons (compounds of carbon and hydrogen only) are the predominant organic compounds in the ambient air that serve as precursors to photochemical oxidants, other volatile organic compounds are also photochemically reactive in those atmospheric processes that give rise to the oxidants. In particular, halogenated organics (e.g., haloalkenes) that participate in photochemical reactions are present in ambient air, although at lower concentrations than the hydrocarbons. They are apparently oxidized through the same initial step involved in the oxidation of the hydrocarbons; that is, attack by hydroxyl radicals (HO·). Alkenes, haloalkenes, and aliphatic aldehydes are, as classes, among the most reactive organic compounds found in ambient air. Alkenic hydrocarbons and halocarbons are unique among VOC in ambient air in that they are susceptible both to attack by HO· and to ozonolysis (oxidation by ozone) (Niki et al., 1983). Methane, halomethanes, and certain haloethenes are of negligible reactivity in ambient air and have been classed as unreactive by the U.S. Environmental Protection Agency (1980).

The oxides of nitrogen that are important as precursors to ozone and other photochemical oxidants are nitrogen dioxide (NO_2) and nitric oxide (NO). Nitrogen dioxide is itself an oxidant that produces deleterious effects, which are the subject of a separate criteria document (U.S. Environmental Protection Agency, 1982a). Nitrogen dioxide is an important precursor to ozone and other photochemical oxidants (1) because its photolysis in ambient air leads to the formation of oxygen atoms that combine with molecular oxygen to form ozone; and (2) because it reacts with acetylperoxy radicals to form peroxyacetyl nitrate (PAN), a relatively potent phytotoxicant (Taylor, 1969; Oshima et al., 1974) and lachrymator (Heuss and Glasson, 1968). Although ubiquitous, nitrous oxide (N_2O) is unimportant in the production of oxidants in ambient air because it is virtually inert in the troposphere. (In the stratosphere, where the wavelength distribution is different, N_2O is photolyzed.)

Since methane is considered only negligibly reactive in ambient air, the volatile organic compounds of importance as oxidant precursors are usually referred to as nonmethane hydrocarbons (NMHC) or, more properly, as nonmethane organic compounds (NMOC).

1.2.2 Measurement of Precursors

Numerous analytical methods have been employed to determine nonmethane organic compounds (NMOC) in ambient air. To present an overview of the most pertinent information, measurement methods for the organic species may be arranged in three major classifications: nonmethane hydrocarbons, aldehydes, and other oxygenated compounds.

Nonmethane hydrocarbons have been determined primarily by methods that employ a flame ionization detector (FID) as the sensing element. Early methods for the measurement of total nonmethane hydrocarbons did not provide for speciation of the complex mixture of organics in ambient air. These methods, still in use for analysis of total nonmethane organic compounds, are essentially organic carbon analyzers, since the response of the FID detector is essentially proportional to the number of carbon atoms present in the organic molecule (Sevcik, 1975). Carbon atoms bound, however, to oxygen, nitrogen, or halogens give reduced relative responses (Dietz, 1967). This detector has been utilized both as a stand-alone continuous detection system (non-speciation) and also with gas chromatographic techniques that provide for speciation of the many organics present in ambient air. A number of studies of non-speciation analyzers have indicated an overall poor performance of the commercial instruments when calibration or ambient mixtures containing NMOC concentrations less than 1 ppm C were analyzed (e.g., Reckner, 1974; McElroy and Thompson, 1975; Sexton et al., 1981). The major problems associated with the non-speciation analyzers have been summarized in a recent technical assistance document published by the U.S. Environmental Protection Agency (1981). The document also presents ways to reduce some of the existing problems.

Because of the above deficiencies, other approaches to the measurement of nonmethane hydrocarbons are currently under development. The use of gas chromatography coupled to an FID system circumvents many of the problems associated with continuous non-speciation analyzers. This method, however, requires sample preconcentration because the organic components are present at part-per-billion (ppb) levels or lower in ambient air. The two main preconcentration techniques in present use are cryogenic collection and the use of solid adsorbents (McBride and McClenny, 1980; Jayanty et al., 1982; Westberg et al., 1980; Ogle et al., 1982). The preferred preconcentration method for obtaining speciated data is cryogenic collection. Speciation methods involving cryogenic preconcentration have also been compared with continuous non-speciation analyzers (e.g., Richter, 1983). Results indicate poor correlation between methods at ambient concentrations below 1 part-per-million carbon (ppm C).

Aldehydes, which are both primary and secondary pollutants in ambient air, are detected by total NMOC and NMHC speciation methods but can not be quantitatively determined by those methods. Primary measurement techniques for aldehydes include the chromotropic acid (CA) method for formaldehyde (Altshuller and McPherson, 1963; Johnson et al., 1981), the 3-methyl-2-benzothiazolone (MBTH) technique for total aldehydes (e.g., Sawicki et al., 1961), Fourier-transform infrared (FTIR) spectroscopy (e.g., Hanst et al., 1982; Tuazon et al., 1978, 1980, 1981b), and high-performance liquid chromatography employing 2,4-dinitrophenyl-hydrazine derivatization (HPLC-DNPH) for aldehyde speciation (e.g., Lipari and Swarin, 1982; Kuntz et al., 1980). The CA and MBTH methods utilize wet chemical procedures and spectrophotometric detection. Interferences from other compounds have been reported for both techniques. The FTIR method offers good specificity and direct _in situ_ analysis of ambient air. These advantages are offset, however, by the relatively high cost and lack of portability of the instrumentation. On the other hand, the HPLC-DNPH method not only offers good specificity but can also be easily transported to field sites. A few intercomparison studies of the above methods have been conducted and considerable differences in measured concentrations were found. The data base is still quite limited at present, however, and further intercomparisons are needed.

Literature reports describing the vapor-phase organic composition of ambient air indicate that the major fraction of material consists of unsubstituted hydrocarbons and aldehydes. With the exception of formic acid, other oxygenated species are seldom reported. The lack of oxygenated hydrocarbon data is somewhat surprising since significant quantities of these species are emitted into the atmosphere by solvent-related industries and since at least some oxygenated species appear to be emitted by vegetation. In addition to direct emissions, it is also expected that photochemical reactions of hydrocarbons with oxides of nitrogen, ozone, and hydroxyl radicals will produce significant quantities of oxygenated products. The adsorptive nature of the surfaces that contact these oxygenated species during sample collection and analysis may account for the apparent lack of data. Attempts have been made to decrease adsorption by deactivating the reactive surface or by modifying the compound of interest (Osman et al., 1979; Westberg et al., 1980). Additional research efforts should focus on this area.

Aside from the essentially unreactive N_2O, only two oxides of nitrogen occur in ambient air at appreciable concentrations: nitric oxide (NO) and nitrogen dioxide (NO_2). Both compounds, together designated as NO_x, participate in the cyclic reactions in the atmosphere that lead to the formation of ozone.

The preferred means of measuring NO and NO_2 is the chemiluminescence method (U.S. Environmental Protection Agency, 1976a,b). The measurement principle is the gas-phase chemiluminescent reaction of O_3 and NO (Fontijn et al., 1970). While NO is determined directly in this fashion, NO_2 is detected indirectly by first reducing or thermally decomposing the gas quantitatively to NO with a converter. The reaction of NO and O_3 forms excited NO_2 molecules that release light energy that is proportional to the NO concentration. Although the NO chemiluminescence is interference-free, other nitrogen compounds do interfere when directed through the NO_2 converter. The magnitude of these interferences is dependent upon the type of converter used (Winer et al., 1974; Joshi and Bufalini, 1976). Other NO and NO_2 measuring methods have also been summarized in Chapter 3. None of the other techniques is widely used to monitor air quality.

1.2.3 Sources and Emissions of Precursors

The photochemical production of ozone, the principal component of "smog," depends both on the presence of precursors, volatile organic compounds (VOCs) and nitrogen oxides (NO_x), that are emitted by manmade and by natural sources, and on suitable conditions of sunlight, temperature, and other meteorological factors. Because of the intervening requirement for meteorological conditions conducive to the photochemical generation of ozone, emission inventories are not as direct predictors of ambient concentrations in the case of secondary pollutants such as ozone and other oxidants as they are for primary pollutants.

Emissions of manmade VOCs (excluding several relatively unreactive compounds such as methane) in the United States have been estimated at 18.2 tg/yr for 1982. Trends in manmade VOC emissions for 1970 through 1982 are shown in Figure 1-1 (U.S. Environmental Protection Agency, 1983). The annual emission rate for manmade VOCs has decreased some 28 percent during this period. The main sources nationwide are industrial processes, which emit a wide variety of VOCs such as chemical solvents; and transportation, which includes the emission of VOCs in gasoline vapor as well as in gasoline combustion products. Estimates of biogenic emissions of organic compounds in the United States are highly inferential but data suggest that the yearly rate is the same order of magnitude as manmade emissions. Biogenic emissions are temperature-dependent and those of isoprene are light-dependent, as well. In addition, isoprene emissions are produced mainly by deciduous trees and therefore should be lower in winter than when the trees have leaves. These factors result in diurnal and seasonal variations in emission rates.

Emissions of manmade NO_x in the United States were estimated at 20.2 tg/yr for 1982. Annual emissions of manmade NO_x were some 12 percent higher in 1982 than in 1970, but the rate leveled off in the late 1970s and exhibited a small decline from about 1980 through 1982. The increase over the period 1970

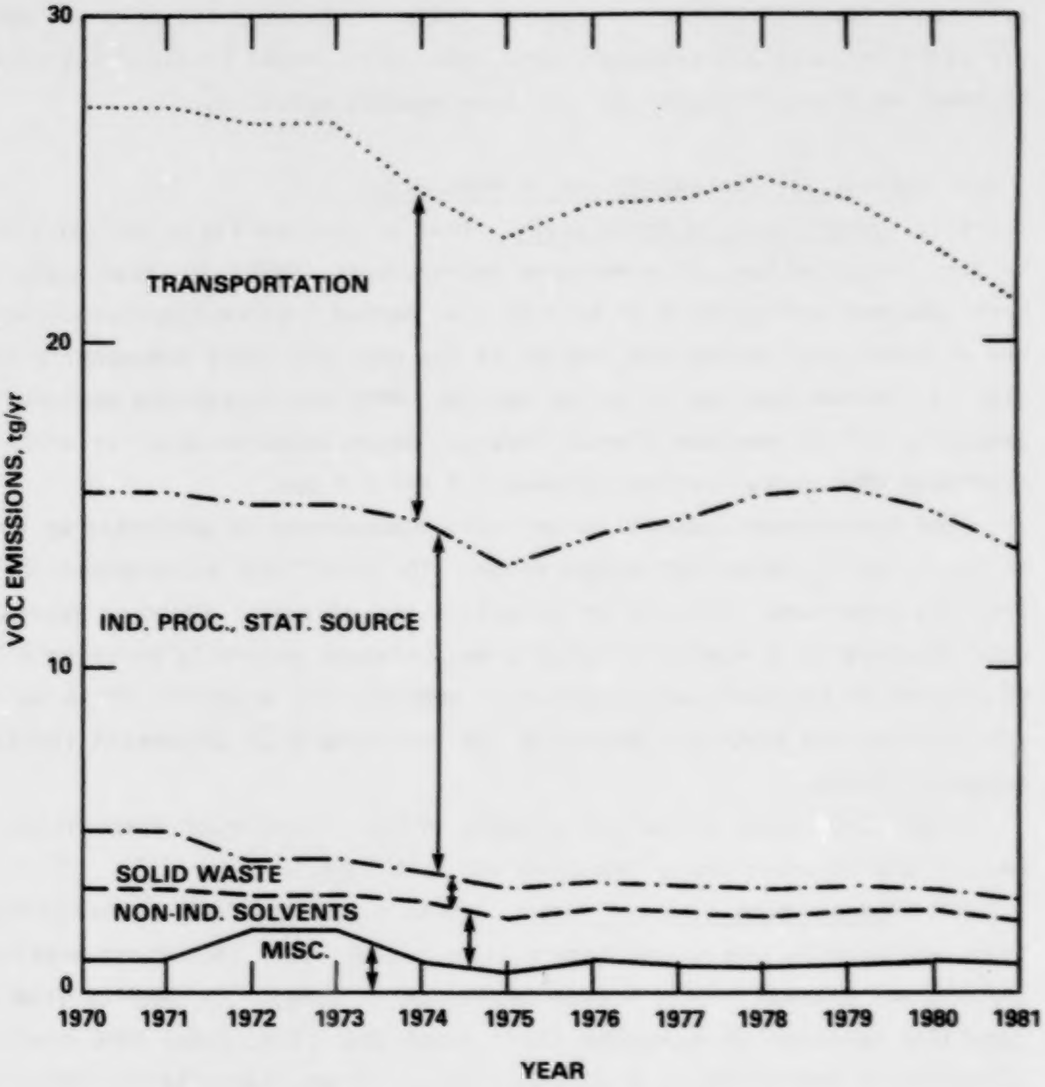

Figure 1-1. National trend in estimated emissions of volatile organic compounds, 1970 through 1982.

Source: U.S. Environmental Protection Agency (1983).

through 1982 had two main causes: (1) increased fuel combustion in stationary sources such as power plants; and (2) increased fuel combustion in highway motor vehicles, as the result of the increase in vehicle miles driven. Total vehicle miles driven increased by 42 percent over the 13 years in question. Trends in manmade NO_x emissions over 1970 through 1982 are shown in Figure 1-2 (U.S. Environmental Protection Agency, 1983). Estimated biogenic NO_x emissions are based on uncertain extrapolations from very limited studies, but appear to be about an order of magnitude less than manmade emissions.

1.2.4 Ambient Air Concentrations of Precursors

1.2.4.1 Hydrocarbons in Urban Areas. Most of the available ambient air data on the concentrations of nonmethane hydrocarbons (NMHC) in urban areas have been obtained during the 6:00 to 9:00 a.m. period. Since hydrocarbon emissions are at their peak during that period of the day, and since atmospheric dispersion is limited that early in the morning, NMHC concentrations measured then generally reflect maximum diurnal levels. Representative data for urban areas show mean NMHC concentrations between 0.4 and 0.9 ppm.

The hydrocarbon composition of urban atmospheres is dominated by species in the C_2 to C_{10} molecular-weight range. The paraffinic hydrocarbons (alkanes) are most prominent, followed by aromatics and alkenes. Based on speciation data obtained in a number of urban areas, alkanes generally constitute 50 to 60 percent of the hydrocarbon burden in ambient air, aromatics 20 to 30 percent, with alkenes and acetylene making up the remaining 5 to 15 percent (Sexton and Westberg, 1984).

Table 1-1 shows a typical example of the hydrocarbon composition in ambient air in urban areas (Westberg and Lamb, 1982).

1.2.4.2 Hydrocarbons in Rural Areas. Rural nonmethane hydrocarbon concentrations are usually one to two orders of magnitude lower than those measured in urban areas (Ferman, 1981; Sexton and Westberg, 1984). In samples from sites carefully selected to guarantee their rural character, total NMHC concentrations ranged from 0.006 to 0.150 ppm C (e.g., Cronn, 1982; Seila, 1981; Holdren et al., 1979). Concentrations of individual species seldom exceeded 0.010 ppm C. The bulk of species present in rural areas are alkanes; ethane, propane, *n*-butane, *iso*-pentane, and *n*-pentane are most abundant. Ethylene and propene are sometimes present at ≤ 0.001 ppm C, and toluene is usually present at ~0.001 ppm C. Monoterpene concentrations are usually about ≤ 0.020 ppm C.

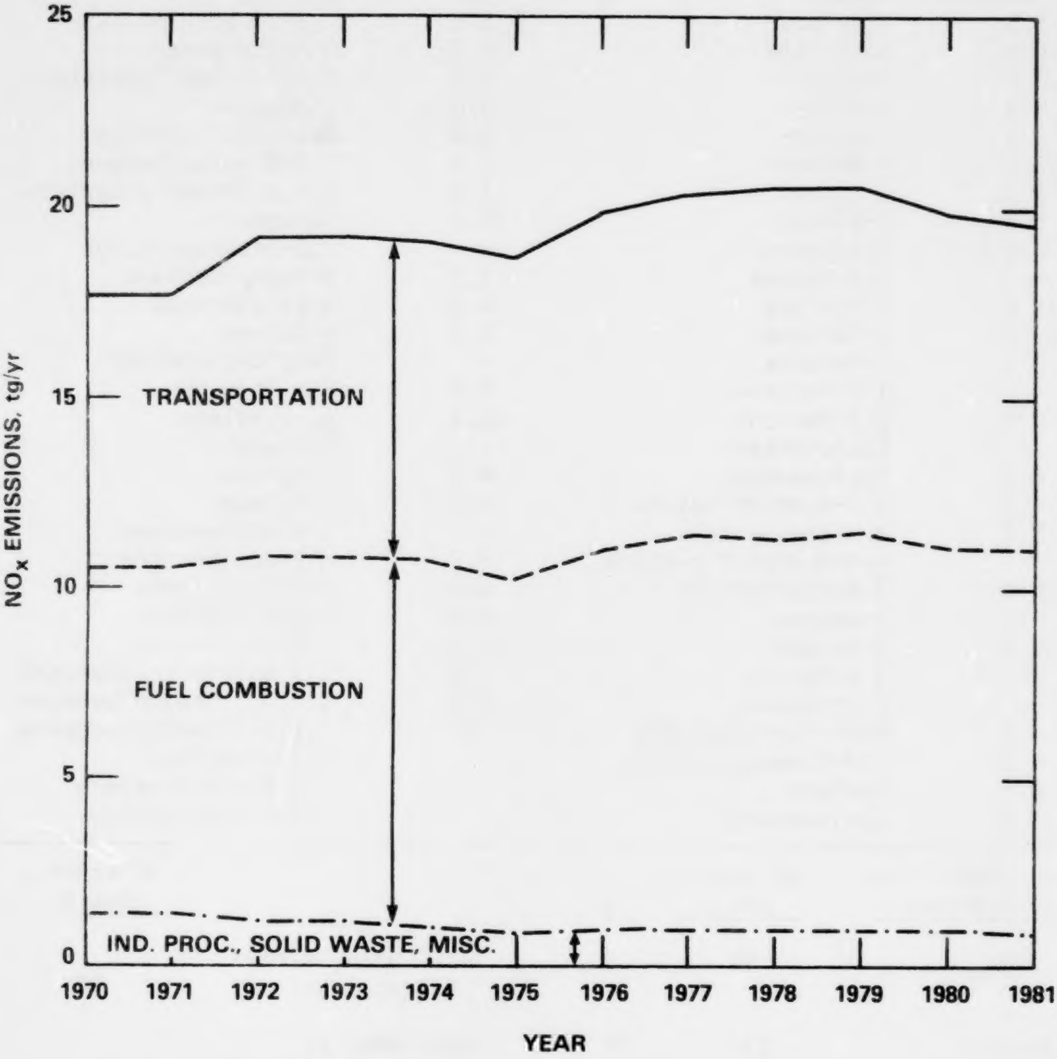

Figure 1-2. National trend in estimated emissions of nitrogen oxides, 1970 through 1982.

Source: U.S. Environmental Protection Agency (1983).

TABLE 1-1. HYDROCARBON (HC) COMPOSITION TYPICALLY MEASURED IN URBAN AREAS (FROM SAMPLE COLLECTED IN MILWAUKEE, 1981)

HC concn., ppb C	Hydrocarbon	HC concn., ppb C	Hydrocarbon
14.0	Ethane	4.5	2-Methylhexane
25.5	Ethylene	5.5	2,3-Dimethylpentane
16.0	Acetylene	8.0	3-Methylhexane
18.5	Propane	5.0	2,2,3-Trimethylpentane
9.5	Propene	8.0	n-Heptane
28.5	i-Butane	3.0	Methylcyclohexane
65.0	n-Butane	1.5	2,4-Dimethylhexane
2.0	1-butene	1.5	2,3,4-Trimethylpentane
3.5	i-Butene	33.5	Toluene
3.5	t-2-Butene	--	2,3-Dimethylhexane
--	c-2-Butene	2.5	2-Methylheptane
49.0	i-Pentane	2.5	3-Ethylhexane
24.0	n-Pentane	2.5	n-Octane
2.0	1-Pentene	--	Ethylcyclohexane
--	t-2-Pentene	6.5	Ethylbenzene
0.5	c-2-Pentene	18.5	p, m-Xylene
--	Cyclopentene	--	Styrene
2.0	Cyclopentane	6.5	o-Xylene
4.5	2,3-Dimethylbutane	4.0	n-Nonane
13.0	2-Methylpentane	--	i-Propylbenzene
--	c-4-Methyl-2-pentene	3.0	n-Propylbenzene
10.0	3-Methylpentane	5.0	p-Ethyltoluene
--	1-Hexene	3.0	m-Ethyltoluene
11.0	n-Hexane	22.0	o-Ethyltoluene
--	t-2-Hexene	3.0	1,3,5-Trimethylbenzene
--	c-2-Hexene	17.0	1,2,4-Trimethylbenzene
6.5	Methylcyclopentane	7.0	1,2,3-Trimethylbenzene
4.5	2,4-Dimethylpentane		Methylstyrene
9.5	Benzene		1,3-Diethylbenzene
2.0	Cyclohexane		1,4-Diethylbenzene

Total identified hydrocarbons	HC concn., ppb c	%		HC concn., ppb C
Σ Olefin	46	9	Total unidentified hydrocarbons	87
Σ Aromatic	134	27	Total NMHC by summing individual species	584
Σ Paraffin	301	60		
Acetylene	16	3		
	497			

Source: Westberg, H.; Lamb, B. (1982)

During the summer months, isoprene concentrations as high as 0.150 ppm C have been measured (Ferman, 1981). The maximum concentrations of isoprene usually encountered, however, are in the range of 0.030 to 0.040 ppm C.

1.2.4.3 Aldehydes in Urban Areas. Aldehydes observed in urban atmospheres include formaldehydes, acetaldehyde, chloral, propanal, *n*-butanal, and benzaldehyde. Formaldehyde concentrations are the best characterized of these aldehydes because the chromotropic acid methodology for formaldehyde was established in the early 1960s. With the exception of early data from Los Angeles (1961), reported concentrations of formaldehyde in urban areas fall in the 0.01 to 0.03 ppm range, with maximum concentrations ranging up to 0.09 ppm.

Comparing these concentrations with concentrations of NMHC in urban areas, it is apparent that formaldehyde probably constitutes less than 3 percent of the total NMOC in most urban areas. Acetaldehyde concentrations are generally lower than formaldehyde in a given urban area. Concentrations of total aldehydes in urban atmospheres can vary from a few ppb up to about 0.2 ppm (200 ppb). In polluted atmospheres, acrolein, propanal, butanal, and benzaldehyde have each been measured at concentrations <0.015 ppm.

1.2.4.4 Aldehydes in Rural Areas. Very few total aldehyde measurements have been made in rural areas. Breeding et al. (1973) reported values for total aldehydes of 0.001 to 0.002 ppm in rural Illinois and Missouri. Formaldehyde levels in remote atmospheres apparently range from 0.1 to 10 ppb, with global background formaldehyde concentrations varying from 0.3 to 0.5 ppb (Duce et al., 1983).

1.2.4.5 Nitrogen Oxides in Urban Areas. Concentrations of NO_x, like hydrocarbon concentrations, tend to peak in urban areas during the early morning, when atmospheric dispersion is limited and automobile traffic is dense. Most NO_x is emitted as nitric oxide (NO), but the NO is rapidly converted to NO_2 by ozone and peroxy radicals produced in atmospheric photochemical reactions. The relative concentrations of NO versus NO_2 fluctuate day-to-day, depending on diurnal and day-to-day fluctuations in ozone levels and photochemical activity.

Urban NO_x concentrations during the 6:00 to 9:00 a.m. period in 10 cities ranged from 0.05 to 0.15 ppm in studies done in the last 5 to 7 years (e.g., Westberg and Lamb, 1983; Richter, 1983; Eaton et al., 1979). Concurrent NMHC measurements for these 10 cities showed that $NMHC/NO_x$ ratios ranged from 5 to 16.

1.2.4.6 Nitrogen Oxides in Rural Areas. Concentrations of NO_x in clean remote environments are usually <0.5 ppb (Logan, 1983). In exceptionally clean air, NO_x concentrations as low as 0.015 ppb have been recorded (Bollinger et al., 1982). Concentrations of NO_x at nonurban sites in the north-central northeastern United States appear to be higher than NO_x concentrations in the west by a factor of 10 (Mueller and Hidy, 1983). From the limited amount of data available, NO_x concentrations in unpopulated rural areas in the west average $\leq$ 1 ppb; but in nonurban northeastern areas average NO_x can exceed 10 ppb.

1.3 CHEMICAL AND PHYSICAL PROCESSES IN THE FORMATION AND OCCURRENCE OF OZONE AND OTHER PHOTOCHEMICAL OXIDANTS

The photochemistry of the polluted atmosphere is exceedingly complex, but an understanding of the basic phenomena is not difficult to acquire. Three processes occur: the emission into the atmosphere of precursors to ozone, from predominantly manmade sources; photochemical reactions that take place during the dispersion and transport of these precursors; and chemical and physical scavenging that reduces the concentrations of ozone (O_3) and other oxidants, and their precursors, along the trajectory. Because transport and dispersion of the precursors together determine the ambient concentrations ozone may finally reach, an understanding of certain meteorological phenomena, in addition to photochemical reactions, is also necessary.

1.3.1 Chemical Processes

In the troposphere, O_3 is formed indirectly through the action of sunlight on nitrogen dioxide (NO_2). In the absence of competing reactions, a steady-state or equilibrium concentration of O_3 is soon established between the O_3, NO_2, and NO (nitric oxide). The injection of organic compounds (primarily hydrocarbons) into the atmosphere upsets the equilibrium and allows the ozone to accumulate at much higher than steady-state concentrations. Recent work on the photochemistry of smog has demonstrated fairly conclusively that the hydroxyl radical, HO·, is the key species in causing organic compounds to play a major role in smog reactions.

The length of the induction period before the accumulation of O_3 begins depends heavily on the initial concentration of HO radicals. There is evidence that nitrous acid (HONO), which is a good source of HO radicals, occurs in the atmosphere, but at very low concentrations. The most important source of HO·, appears, rather, to be aldehydes, which are constituents of automobile exhaust, as well as decomposition products of most atmospheric photochemical reactions involving hydrocarbons.

The occurrence of organic compounds and sunlight does not mean that the photochemical reactions will continue indefinitely. Terminating reactions gradually remove NO_2 from the reaction mixtures, such that the photochemical cycles would slowly come to an end unless fresh NO and NO_2 emissions were injected into the atmosphere. Besides ozone, other oxidants that contain nitrogen, such as peroxyacetyl nitrate (PAN), nitric acid (HNO_3), and peroxynitric acid (HNO_4), as well as organic nitrates and inorganic nitrates, are some of the terminating compounds.

The maximum concentration that O_3 can reach in polluted atmospheres appears to depend on the hydrocarbon-nitrogen oxides ratio. At a low ratio (1:1 to 2:1), insufficient HO· radicals are available from the hydrocarbon species to effect the conversion of NO to NO_2, a necessary first step. At high ratios (greater than 12:1 to 15:1), conversion of NO to NO_2 occurs rapidly, but the terminating reactions remove NO_2 from the reaction cycles and O_3 cannot build up to high concentrations. Only at intermediate ratios (4:1 to 10:1) are conditions favorable to the formation of appreciable concentrations of O_3.

Recent studies on the fundamental photochemistry of organic compounds have been reasonably successful. The reactions of paraffinic compounds (alkanes) are fairly well understood, as are those of olefinic compounds (alkenes). Photochemical reactions of the aromatic compounds, however, are poorly understood.

Natural hydrocarbons (i.e., those organic compounds emitted from vegetation), as well as hydrocarbons from manmade sources, can react photochemically with nitrogen oxides to yield O_3, although natural hydrocarbons are reported to be mainly scavengers of O_3 rather than producers of O_3.

Besides direct adverse effects on human health and on vegetation, O_3 contributes to visibility degradation and to acidic deposition. Through its photolysis by sunlight, with subsequent generation of HO radicals, ozone participates only indirectly, but not insignificantly, in the formation of both sulfate and nitrate aerosols, which cause reduced visibility. These sulfate and nitrate species, on further reaction, result in acidic deposition.

1.3.2 Physical Processes

Meteorological processes are quite important in determining the extent to which O_3 precursors can accumulate, and thereby the concentration of O_3 that can result. Atmospheric mixing depends principally on the amount of turbulent mixing, wind speed and direction, or all three. Geography can have a significant impact, also, particularly at land-sea interfaces.

The degree of turbulent mixing can be characterized by atmospheric stability. Pollutants do not spread rapidly in stable layers, nor do they mix upwards rapidly through stable layers to higher altitudes. Rather, stable layers are usually characterized by temperature inversions, in which the temperature increases with increasing altitude. Since pollutants emitted below or into an inversion layer will not readily mix across the inversion layer, they may persist for a considerable time and distance until the inversion is broken, usually by surface heating resulting from sunlight.

The extent to which surface heating can cause mixing heights to increase (and to cause dilution of O_3 and its precursors) is highly dependent on geography. Along both the Pacific Coast and the Northeast Coast, as well as near the Great Lakes, low-level inversions (i.e., the mixing height is not great) frequently persist through the afternoon, making these areas prone to local and regional air pollution episodes.

Wind speed and direction determine the extent to which pollutants can be increased by passing over successive sources, or can be diluted by being rapidly removed from the source area. The plumes of precursors and resulting O_3 from large metropolitan areas have been shown to persist for hundreds of miles. Three kinds of transport of ozone and other pollutants have been described, in terms of transport distance. In urban-scale transport, maximum concentrations of O_3 are produced about 20 miles or so (and about 2 to 3 hours) downwind from the major pollutant source areas. In mesoscale transport, O_3 has been observed up to 200 miles downwind from the sources of its precursors. Synoptic-scale transport is associated with large-scale, high-pressure air masses that may extend over and persist for many hundreds of miles.

The significance of sunlight in photochemistry is related to its intensity and its spectral distribution, both of which have direct effects on the specific chemical reaction steps that initiate and sustain oxidant formation. Days on which significant ozone-oxidant concentrations occur are usually days with warm, above-normal temperatures. These are also characteristic of high pressure systems with inversions and low winds. The photolysis of aldehydes is affected by the spectral distribution of light, since it is strongly dependent on wavelength in the near ultraviolet region.

Ozone formed in the stratosphere can be brought downwards to the earth's surface by events called "tropopause folds." These events are most commonly observed in the mid-latitudes during spring and early summer. Relatively high concentrations of O_3 can occur for short periods of time, minutes to a few hours, over local areas.

1.4 PROPERTIES, CHEMISTRY, AND MEASUREMENT OF OZONE AND OTHER PHOTOCHEMICAL OXIDANTS

1.4.1 Properties

Ozone, peroxyacetyl nitrate, and hydrogen peroxide, along with other photochemical oxidants occurring at very low concentrations in ambient air, are characterized chiefly by their ability to remove electrons from or to share electrons with other molecules or ions (i.e., oxidation). The capability of a chemical species for oxidizing or reducing other chemical species is termed "redox potential" (positive or negative standard potential) and is expressed in volts. Ozone has a standard potential of +2.07 volts in aqueous systems (for the redox pair, O_3/H_2O). Hydrogen peroxide has a standard potential of +1.776 in the redox pair, H_2O_2/H_2O. No standard potential for peroxyacetyl nitrate in neutral or buffered aqueous systems, such as those that occur in biological systems, appears in the literature. In acidic solution (pH 5 to 6), PAN hydrolyzes fairly rapidly; in alkaline solution it decomposes with the production of nitrite ion and molecular oxygen.

The toxic effects of oxidants are attributable to their oxidizing ability. Their oxidizing properties also form the basis of the measurement techniques for all three of these pollutants. The calibration of ozone and PAN measurements, however, is achieved via their spectra in the ultraviolet and infrared, respectively. The calibration of measurement methods for H_2O_2 is achieved with iodometric techniques that depend on the oxidizing properties of H_2O_2.

An important property of PAN, especially in the laboratory, is its thermal instability. Its explosiveness dictates its synthesis for calibration purposes by experienced personnel only. All three pollutants must be generated in situ for the calibration of measurement techniques. For ozone and H_2O_2, generation of calibration gases is reasonably straightforward.

1.4.2 Reactions of Ozone and Other Oxidants in Ambient Air

The atmospheric reactions of ozone and of other photochemical oxidants such as peroxyacetyl nitrate (PAN) and hydrogen peroxide (H_2O_2) are complex and diverse, but are becoming increasingly well-characterized. The reactions of these species result in products and processes that may have significant environmental and health- and welfare-related implications, including effects on biological systems, nonbiological materials, and such phenomena as visibility degradation and acidification of cloud and rain water. Ozone may play a role in the oxidation of SO_2 to H_2SO_4, both indirectly in the gas phase (via formation of OH radicals and Criegee biradicals) and directly in aqueous droplets. Evidence is also accumulating that hydrogen peroxide, like ozone, is involved in both gas-phase photochemistry and aqueous-phase oxidations. For example, studies of the rates of oxidation of SO_2 by H_2O_2 in solution suggest that this reaction is sufficiently fast that it could be the major aqueous-phase route for the oxidation of SO_2 under certain atmospheric conditions. In addition, the importance of oxidants such as PAN in various aspects of atmospheric chemistry, such as long-range transport of NO_x and multi-day air pollution episodes, is now being recognized.

Ozone can react with organic compounds in the troposphere. It is important to recognize, however, that organics undergo competing reactions with OH radicals in the daytime (Atkinson et al., 1979; Atkinson and Lloyd, 1984) and, in certain cases, with NO_3 radicals during the night (Japar and Niki, 1975; Carter et al., 1981; Atkinson et al., 1984a,b,c,d), as well as photolysis. Only for organics whose ozone reaction rate constants are greater than $\sim 10^{-21}$ cm^3 $molecule^{-1}$ sec^{-1} can consumption by ozone be considered to be atmospherically important (Atkinson and Carter, 1984).

Ozone reacts rapidly with the acyclic mono-, di-, and tri-alkenes and with cyclic alkenes. The rate constants for these reactions range from $\sim 10^{-18}$ to $\sim 10^{-14}$ cm^3 $molecule^{-1}$ sec^{-1} (Atkinson and Carter, 1984), corresponding to atmospheric lifetimes ranging from a few minutes for the more reactive cyclic alkenes, such as the monoterpenes, to several days. In polluted atmospheres, a significant portion of the consumption of the more reactive alkenes will occur via reaction with ozone, rather than with OH radicals, especially in the afternoons during photochemical oxidant episodes. Reactions between ozone and alkenes can result in aerosol formation (National Academy of Sciences, 1977; Schuetzle and Rasmussen, 1978), with alkenes of higher carbon numbers the chief contributors.

Because of their respective rate constants, neither alkanes (Atkinson and Carter, 1984) nor alkynes (Atkinson and Aschmann, 1984) are expected to react with ozone in the atmosphere, since competing reactions with OH radicals have higher rate constants.

The aromatics react with ozone, but quite slowly (Pate et al., 1976; Atkinson et al., 1982), such that their reactions with ozone are expected to be unimportant in the atmosphere. Cresols are more reactive toward ozone than the aromatic hydrocarbons (Atkinson et al., 1982), but their reactions with OH radicals (Atkinson et al., 1978, 1982) or NO_3 radicals (Carter et al., 1981; Atkinson et al., 1984a) predominate.

For oxygen-containing organic compounds, especially those without carbon-carbon double bonds, reactions with ozone are slow. For carbonyls and ethers (other than ketene) that contain unsaturated carbon-carbon bonds, however, much faster reactions are observed (Atkinson et al., 1981).

The kinetics of the reactions of ozone with a variety of nitrites, nitriles, nitramines, nitrosamines, and hydrazines have been studied (Atkinson and Carter, 1984), but only for the hydrazines are these reactions sufficiently rapid to be of atmospheric importance. Chamber studies have shown that N-nitrosodimethylamine can result from the reaction of ozone with simple hydrazines (Tuazon et al., 1981). Whether this product would ever be formed by reaction with ozone in the atmosphere obviously depends upon the presence, and level, of the precursor hydrazines in ambient air.

Certain reactions of ozone other than its reactions with organic compounds are important in the atmosphere. Ozone reacts rapidly with NO to form NO_2, and subsequently with NO_2 to produce the nitrate (NO_3) radical and an oxygen molecule. Photolysis of ozone can be a significant pathway for the formation of OH radicals, particularly in polluted atmospheres when ozone concentrations are at their peak.

1.4.3 Reactions of Ozone and Peroxyacetyl Nitrate in Aqueous (Biological) Systems

Both ozone and PAN can react directly and rapidly with many organic molecules, including many types occurring in biological systems. Additionally, active species such as singlet oxygen, hydroxyl radicals, and superoxide are produced either as products of primary reactions or from the decomposition of ozone or PAN in water; these species also have the potential for causing biological damage.

The reactions of ozone with biologically important functional groups have been described in the literature, although such information remains relatively sparse and is based on *in vitro* work that is not always pertinent to reactions that occur under the conditions of *in vivo* exposure. Among the functional groups with which ozone reacts relatively rapidly are the carbon-carbon double bonds (alkenic group) found in biologically important compounds such as some of the essential fatty acids and polyunsaturated fatty acids (PUFA) of the kind found in the lipids of cell membranes. Amines are, in general, close to alkenes in their reactivity toward ozone, although amino groups existing as the amide or salt are less susceptible to ozone than unprotected amino groups. Sulfur-containing compounds, such as methionine, can also undergo electrophilic attack by ozone, resulting in the formation of both sulfoxides and sulfones. Under some conditions (e.g., pH > 9), ozone is rapidly converted to hydroxyl radicals, which are less selective than ozone in reactions with organic molecules. The conversion of ozone to superoxide ($O_2\cdot$) and hydroperoxy radicals ($HO_2\cdot$) has also been reported.

Aromatic compounds are much less reactive toward ozone than alkenic compounds in aqueous systems. In compounds containing both aromatic and alkenic groups, such as the indole ring of tryptophan, the initial ozone attack occurs exclusively at the alkenic part of the molecule. Aldehydes react with ozone with and without the involvement of oxygen. Either way, acyl hydrotrioxides are formed that subsequently decompose to peroxides and carboxylic acids. Simple ketones react slowly or not at all with ozone.

Reactions between ozone and specific molecules of importance in biological systems have been described in Chapter 10.

Knowledge of the solution chemistry of PAN is limited. It is known, however, that PAN can react with alkenes, with sulfur-containing compounds, and with aldehydes. The half-life of PAN in water (pH 7.2) is only about 4.4 minutes. Thus, some of the toxicological effects ascribed to PAN should possibly be attributed to its decomposition products instead.

1.4.4 Sampling and Measurement of Ozone and Other Photochemical Oxidants

The analysis of ozone and other, related atmospheric oxidants includes requirements for representative sampling, specific and sensitive measurement methodologies, methods for the generation of standard samples, absolute methods for the calibration of these standards, and procedures by which to provide quality assurance for the whole measurement process. In the summary presented below, recommended procedures are given for all of these analytical steps. Sampling and quality assurance are discussed in general terms for all of the oxidants. Methods of analysis, sampling, and generation and calibration are discussed specifically for ozone, peroxyacetyl nitrate (PAN) and its homologues, and hydrogen peroxide. Because of the large existing data base that employed measurements for "total oxidants," non-specific iodometric techniques are discussed and compared to current specific O_3 measurements.

1.4.4.1 Quality Assurance and Sampling. A quality assurance program is employed by the U.S. Environmental Protection Agency for assessing the accuracy and precision of monitoring data and for maintaining and improving the quality of ambient air data. Procedures and operational details have been prescribed in each of the following areas: selection of analytical methods and instrumentation (i.e., reference and equivalent methods); method specifications for gaseous standards; methods for primary and secondary (transfer standards) calibration; instrumental zero and span check requirements, including frequency of cohorts, multiple-point calibration procedures, prevention and remedial maintenance requirements; procedures for air pollution episode monitoring; methods for recording and validating data; and information on documentary quality control (U.S. Environmental Protection Agency, 1977a).

A crucial link in the measurement cycle involves sampling strategies and techniques. Sampling strategies, which involve the design and operation of a sampling network, must be consistent with the specific purpose of the measurements. Ambient air monitoring data are collected for a variety of purposes, each of which may have different requirements that affect sampling strategy. For example, a sampling strategy for health effects research studies may require a number of monitoring stations carefully situated to assess human exposure for a given urban population over a finite period of time. In addition, since ozone, PAN, and H_2O_2 are all secondary pollutants formed after an initial induction period, stations for monitoring peak concentrations should be located downwind of the urban center of precursor emissions.

The reactivity and instability of O_3 and other photochemical oxidants dictate special sampling techniques. Samples of air containing O_3 cannot be collected and stored and must be analyzed dynamically. Analysis for PAN must likewise be performed as soon as possible after collection. Hydrogen peroxide collected in aqueous media is fairly stable, but samples are subject to interfering reactions from ozone trapped in solution. Sampling probes should be constructed of Teflon or some similarly inert material, and inlet residence times should be as short as possible. Other design criteria for O_3 monitoring stations have been given (Standing Air Monitoring Work Group, 1977; National Academy of Sciences, 1977). The most important of these are that inlets of the sampling probe should be positioned 3 to 15 m (10 to 49 ft) above ground and at least 4 m (13 ft) from large trees and 120 m (349 ft) from heavy automobile traffic.

1.4.4.2 Measurement Methods for Total Oxidants and Ozone. Techniques for the continuous monitoring of total oxidants and O_3 in ambient air are summarized in Table 5-13. The earliest methods used for routinely monitoring oxidants in the atmosphere were based on iodometry. When atmospheric oxidants are absorbed in potassium iodide (KI) reagent, the iodine produced,

$$O_3 + 3I^- + H_2O = I_3^- + O_2 + 2OH^- \qquad (1\text{-}1)$$

is measured by ultraviolet absorption in colorimetric instruments and by amperometric means in electrochemical instruments. The term "total oxidants" is of historical significance only and should not be construed to mean that such measurements yield a sum of the concentrations of the oxidants in the atmosphere. The various oxidants in the atmosphere react to yield iodine at different rates and with different stoichiometries. Only ozone reacts immediately to give a quantitative yield of iodine. Hydrogen peroxide, for example, produces iodine at a slow rate and because of its low concentration compared to ozone would be expected to have little effect upon a total oxidants measurement. As discussed below, the total oxidants measurement correlates fairly well with the specific measurement of ozone, except during periods when significant NO_2 and SO_2 interferences are present. The major problem with the total oxidants measurement was the effect of these interferences. Total oxidants instruments have now been replaced by specific ozone monitors in all aerometric networks and in most research laboratories. Biases among and between "total oxidants" and ozone methods are still important, however, for evaluating existing data on health and welfare "effects levels" where concentrations were measured by "total oxidants" methods.

The reference method promulgated by EPA for compliance monitoring is the chemiluminescence technique based on the gas-phase ozone-ethylene reaction (U.S. Environmental Protection Agency, 1971b). The technique is specific for ozone, the response (luminescence intensity) is a linear function of concentration, detection limits of 0.001 to 0.005 ppm are readily obtained, and response times of 30 seconds or less are readily obtained. Prescribed methods of testing and prescribed performance specifications that a commercial analyzer must meet in order to be designated as a reference method or an equivalent method have been published by EPA (U.S. Environmental Protection Agency, 1975). An analyzer may be designated as a reference method if it is based on the same principle as the reference method and meets performance specifications. Commercial analyzers that have been designated as reference methods were listed in Chapter 5 (Table 5-7). An acceptable equivalent method must meet the prescribed performance specifications and also show a consistent relation with the reference method. Commercial analyzers that have been designated as equivalent methods were also listed in Chapter 5 (Table 5-7).

The designated equivalent methods are based on either the gas-solid chemiluminescence procedure or the ultraviolet absorption procedures (Table 1-2). The first designated equivalent method was based on ultraviolet absorption of the mercury 254 nm emission line. The absorption coefficient of ozone is accurately known at this wavelength with an accepted value of 134 M^{-1} cm^{-1}. Detection limits of 0.005 ppm are readily obtained by modern digital capabilities for making precise measurements of weak absorbancies at moderate pathlengths. Compensation for potential interferences that also absorb at 254 nm is made by comparing an averaged transmission signal of ozone in air to the transmission signal through an otherwise identical air sample from which the ozone has been preferentially scrubbed. Advantages of this UV absorption technique are that a reagent gas is not required and control of sample air flow is not critical. In addition, the measurement is in principle an absolute one, in that the ozone concentration can be computed from the measured transmission signal since the absorption coefficient and pathlength are accurately known.

In the gas-solid chemiluminescence analyzer, the reaction between ozone and Rhodamine-B adsorbed on activated silica produces chemiluminescence, the intensity of which is directly proportional to ozone concentration. The sensitivity is greater than the gas-phase chemiluminescence method and a controlled reagent gas flow is not required. The sensitivity of the reaction surface decays gradually with time, but the analyzer contains internal means to compensate for the decay.

TABLE 1-2. SUMMARY OF OZONE MONITORING TECHNIQUES

Principle	Reagent	Response	Minimum detection limit	Response time, 90% FS[a]	Major interferences	References
Continuous colorimetric	10(20)% KI buffered at pH = 6.8	Total oxidants	0.010 ppm	3 to 5 minutes	NO_2(+20%, 10%RI) SO_2(-100%)	Littman and Benoliel (1953) Tokiwa et al. (1972)
Continuous electrochemical	2% KI buffered at pH = 6.8	Total oxidants	0.010 ppm	1 minute	NO_2(+6%) SO_2(-100%)	Brewer and Milford (1960) Mast and Saunders (1962) Tokiwa et al. (1972)
Chemiluminescence	Ethylene, gas-phase	O_3-specific	0.005 ppm	< 30 seconds	None[b]	Nederbragt et al. (1965) Stevens and Hodgeson (1973)
Chemiluminescence	Rhodamine-B	O_3-specific	0.001 ppm	< 1 minute	None	Regener (1960, 1964) Hodgeson et al. (1970)
Ultraviolet photometry	None	O_3-specific	0.005 ppm	30 seconds	Species that absorb at 254 nm[c]	Bowman and Horak (1972)

[a] FS = full response.

[b] A signal enhancement of 3 to 12% has been reported for measurement of O_3 in humid versus dry air (California Air Resources Board, 1976).

[c] No significant interferences have been reported in routine ambient air monitoring. If abnormally high concentrations of species that absorb at 254 nm (e.g., aromatic hydrocarbons and mercury vapor) are present, some positive response may be expected. If high aerosol concentrations are sampled, inlet filters must be used to avoid a positive response.

1.4.4.3 Calibration Methods. All the analyzers discussed above must be periodically calibrated with ozonized air streams, in which the ozone concentration has been determined by some absolute technique. This includes the UV absorption analyzer, which, when used for continuous ambient monitoring, may experience ozone losses in the inlet system because of contamination.

An ozone calibration system for a primary laboratory calibration system consists of a clean air source, an ozone generator, and a sampling manifold. The ozone generator most often used is a photolytic source employing a mercury pen-ray lamp that irradiates a quartz tube through which clean air flows at a controlled rate (Hodgeson et al., 1972). The ozone concentration may be varied by means of a mechanical sleeve over the lamp envelope or by changing the lamp voltage or current. Once the output of the generator has been calibrated by a primary reference method, it may be used to calibrate O_3 transfer standards, which are portable generators, instruments, or other devices used to calibrate analyzers in the field. Reference calibration procedures that have been used for total oxidants and ozone-specific analyzers in this country are summarized in Table 1-3.

The original reference calibration procedure promulgated by EPA was the 1 percent neutral buffered potassium iodide (NBKI) method (U.S. Environmental Protection Agency, 1971). This technique was employed in most of the United States, with the exception of California, which routinely used a 2 percent NBKI procedure that was quite similar to the EPA method except for the use of humidified air through the ozone source (California Air Resources Board, 1976). The Los Angeles Air Pollution Control District (LAAPCD) used a 1 percent unbuffered KI procedure and measured the iodine produced by a titration technique rather than the photometric technique used in the California and EPA methods. A number of studies conducted between 1974 and 1978 revealed several deficiencies with KI methods, the most notable of which were poor precision or interlaboratory comparability and a positive bias of NBKI measurements relative to simultaneous absolute UV absorption measurements. The positive bias was also observed with respect to gas-phase titration (GPT) of ozone with standard nitric oxide (NO) samples. The positive bias observed is peculiar to the use of phosphate buffer in the NBKI techniques. The bias was not observed in the unbuffered LAAPCD method (which nevertheless suffered from poor precision), nor in the 1 percent EPA KI method without phosphate buffer (Hodgeson et al., 1977), nor in a KI procedure that used boric acid as buffer (Flamm, 1977). A summary

TABLE 1-3. OZONE CALIBRATION TECHNIQUES

Method	Reagent	Primary standard[a]	Method used, organization, and dates	Purpose	Bias, $[O_3]_i/[O_3]_{uv}$
1% NBKI	1% KI, phosphate buffer pH = 6.8	Reagent grade arsenious oxide	EPA 1971-1976	Primary reference procedure	1.12 ± 0.05[b]
2% NBKI	2% KI phosphate buffer pH = 6.8		CARB until 1975	Primary reference procedure	1.20 ± 0.05[b]
1% Unbuffered KI	1% KI pH = 7		LAAPCD until 1975	Primary reference procedure	0.96[c]
UV photometry	None	O_3 absorptivity at Hg 254 nm emission line	All 1979-present	Primary reference procedure[d]	
Gas-phase titration (GPT)	No standard reference gas	No SRM (50 ppm in N_2) from NBS	EPA, States 1973-present	Alternative reference procedure (1973-1979) Transfer standard (1979-present)	1.030 ± 0.015[e]
1% BAKI	1% KI, boric acid buffer pH = 5	Standard KIO_3[f] solutions	EPA 1975-1979	Alternative reference procedure	1.00 ± 0.05

[a] In the case of the iodometric methods, the primary standard is the reagent used to prepare or standardize iodine solutions.

[b] The uncertainty limits represent the range of values obtained in several independent studies.

[c] Only one study available (Demore et al., 1976).

[d] UV photometry used as reference method by CARB since 1975. This technique used as an interim, alternative reference procedure by EPA from 1976 to 1979.

[e] This is the value reported in the latest definitive study (Fried and Hodgeson, 1982). Previous studies reported biases ranging from 0 to 10 percent (Burton et al., 1976; Paur and McElroy, 1979).

[f] This procedure also recommended a standard I_3^- solution absorptivity to be used instead of the preparation of standard iodine solutions.

of results of these prior studies was presented in the previous criteria document (U.S. Environmental Protection Agency, 1978a) and in a review by Burton et al. (1976). Correction factors for converting NBKI calibration data to a UV photometry basis were given in Chapter 5.

Subsequently, EPA evaluated four alternative reference calibration procedures based on UV photometry, GPT with excess NO, GPT with excess ozone and the boric acid buffered KI technique (BAKI). The results of these studies (Rehme et al., 1981) showed that UV photometry was superior in accuracy, precision, and simplicity of use; and in 1979 regulations were amended to specify UV photometry as the reference calibration procedure (U.S. Environmental Protection Agency, 1979a,b,c,d). Laboratory photometers used as reference systems for absolute O_3 measurements have been described by Demore and Patapoff (1976), Bass et al. (1977), and Paur and Bass (1983).

These laboratory photometers contain long path cells (1 to 5 m) and employ sophisticated digital techniques for making effective double beam measurements of small absorbancies and low ozone concentrations. A primary standard UV photometer, such as those above, is one that meets the requirements and specifications given in the revised ozone calibration procedures (U.S. Environmental Protection Agency, 1979d). Since these are currently available in only a few laboratories, EPA has allowed the use of transfer standards, which are devices or methods that can be calibrated against a primary standard and transferred to another location for calibration of O_3 analyzers. Examples of transfer standards that have been used are commercial O_3 photometers, calibrated generators, and GPT apparatus. Guidelines on transfer standards have been published by EPA (McElroy, 1979).

1.4.4.4 Relationship of Total Oxidants and Ozone Measurements. The temporal and quantitative relationship between simultaneous total oxidants and ozone measurements has been examined in this chapter because of the existence of a data base obtained by "total oxidants" measurements. Such a comparison is complicated by the relative scarcity of data, the presence of both positive (NO_2) and negative (SO_2) interferences in total oxidants measurements, and the change in the basis of calibration. In particular, the presence of NO_2 and SO_2 interferences prevents the establishment of a definite quantitative relationship between ozone and oxidants data. Nevertheless, some interesting conclusions can be drawn and are summarized below.

An expected relationship between total oxidants and specific O_3 measurements can be predicted based upon the known response of oxidant instrumentation to oxidizing and reducing species in the atmosphere. The predicted relation in this document assumes that NO_2 is the only significant positive interference and that SO_2 is the predominant negative interference. Because of the potential presence of oxidizing (NO_2) and reducing (SO_2) interferences, it is difficult or impractical to intercompare measurements during evening and early morning hours when ozone concentrations are at a minimum. The relationship is best compared at the midday to early afternoon diurnal maximum of ozone when NO_2 concentrations are approaching a minimum; the SO_2 concentration at this time will depend on local emissions. A comparison of maximum hourly averages is appropriate since the primary and secondary ambient air quality standards are based on this value. If legitimate corrections or compensations have been made for SO_2 and NO_2 interferences, the corrected total oxidants concentrations should always be higher than simultaneous O_3 concentrations by an amount dependent on type and concentrations of other oxidants present. The major other oxidants known to exist in the atmosphere are PAN and H_2O_2. Maximum concentrations of these oxidants occur near the ozone diurnal maximum (Chapter 6) with values that are only a fraction of the O_3 maximum (section 6.6 and 6.7). In addition, both of these are classified as slow oxidants in that they release iodine at a slow rate in aqueous solution. Therefore, if a contribution from these species is discernible at all in the total corrected oxidants reading, it should be only a small fraction of the ozone contribution. For most of the aerometric data base, particularly outside the state of California, no attempts were made to correct total oxidants concentrations for NO_2 and SO_2 because such corrections were impractical or impossible. For uncorrected total oxidants data, the counterbalancing effects of SO_2 and NO_2 interferences make it even more difficult to discern contributions from oxidants other than ozone. The uncorrected total oxidants data should then be either higher than or lower than corresponding ozone data, depending on the relative concentrations of SO_2 and NO_2.

The simultaneous comparisons that have been made in large part confirm the predictions above. Studies concluded in the early to mid-1970s were reviewed in the previous criteria document (U.S. Environmental Protection Agency, 1978a). Averaged data showed fairly good qualitative and quantitative agreement between diurnal variations of total oxidants and ozone. Uncorrected data showed distinct morning and evening peaks resulting from NO_2 interference. Data taken from individual days of respective studies showed considerably more variation, with total oxidants measurements both higher and lower than ozone measurements.

The most recent comparison in the literature involved simultaneous ozone and total oxidant measurements in the Los Angeles basin by the California Air Resources Board (1978) in 1974, 1976, and 1978. The maximum hourly data pairs were correlated (Chock et al., 1982) and yielded the following regression equation for 1978, in which a large number (927) of data pairs were available:

$$\text{Oxidant (ppm)} = 0.870\ O_3 + 0.005$$
$$\text{(Correlation coefficient} = 0.92) \qquad (1\text{-}2)$$

The oxidant data were uncorrected for NO_2 and SO_2 interferences, and, again, on individual days maximum oxidant averages were both higher than and lower than ozone averages.

In summary, specific ozone measurements agree fairly well with total oxidants corrected for NO_2 and SO_2 interferences, and in such corrected total oxidants measurements ozone is the dominant contributor to total oxidants. Indeed, it is difficult to discern the presence of other oxidants in most total oxidant data. There can, however, be major temporal discrepancies between ozone and oxidants data, which are primarily a result of oxidizing and reducing interferences with KI measurements. As a result of these interferences, on any given day the total oxidant values may be higher than or lower than simultaneous ozone data. The measurement of ozone is a more reliable indicator than total oxidant measurements of oxidant air quality.

1.4.4.5 Methods for the Sampling and Analysis of Peroxyacetyl Nitrate and Its Homologues.

Only two analytical techniques have been used to obtain significant data on ambient peroxyacetyl nitrate (PAN) concentrations. These are gas chromatography with electron capture detection (GC-ECD) and long-path Fourier transform infrared (FTIR) spectrometry. Atmospheric data on PAN concentrations have been obtained predominantly by GC-ECD because of its relative simplicity and superior sensitivity. These techniques have been described in this chapter along with attendant methods of sampling. Since PAN is thermodynamically unstable, standards must be generated and analyzed by some absolute technique for the purpose of calibrating the GC-ECD. Thus, PAN generation techniques and absolute methods for analyzing these samples have also been summarized.

By far the most widely used technique for the quantitative determination of ppb concentrations of PAN and its homologues is GC-ECD (Stephens, 1969). With carbowax or SE30 as a stationary phase, PAN, peroxypropionyl nitrate (PPN), peroxybenzoyl nitrate (PBzN), and other homologues (e.g., peroxybutyrl nitrate) are readily separated from components such as air, water, and other atmospheric compounds, as well as ethyl nitrate, methyl nitrate, and other contaminants that are present in synthetic mixtures. Electron-capture detection provides sensitivities in the ppb and sub-ppb ranges. Table 1-4 shows parameters used by several investigators to determine trace levels of PAN by GC-ECD. Sample injection into the GC is accomplished by means of a gas-sampling valve with a gas-sampling loop of a few milliliters' volume. Sample injection may be performed manually or automatically. Typically, manual air samples are collected in 50-200 ml ungreased glass syringes and purged through the gas-sampling valve. Samples collected from the atmosphere should be analyzed as soon as possible because PAN and its homologues undergo thermal decomposition in the gas phase and at the surface of containers.

The recent work of Singh and Salas (1983a, 1983b) on the measurement of PAN in the free (unpolluted) troposphere (see Chapter 6) is illustrative of current capabilities for measuring low concentrations. A minimum detection limit of 0.010 ppb was obtained. The literature contains conflicting reports on the effects of variable relative humidity on PAN measurements by GC-ECD. Some investigators have reported a reduced response to PAN calibration samples when dry diluent gas is used, whereas others have not observed this effect. The reduced response has been attributed to losses of PAN to surfaces within the inlet system and the GC. Presumably, water vapor may deactivate surfaces. For the present, if a moisture effect is suspected in a PAN analysis, the bulk of this evidence suggests that humidification of PAN calibration samples (to a range approximating the humidity of the samples being analyzed) would be advisable.

Conventional long-path infrared spectroscopy and Fourier-transform infrared spectroscopy (FTIR) have been used to detect and measure atmospheric PAN. Sensitivity is enhanced by the use of FTIR. The most frequently used IR bands have been assigned and the absorptivities shown in Table 1-5 permit the quantitative analysis of PAN without calibration standards. The absorptivity of the 990 cm^{-1} band of PBzN has been reported by Stephens (1969). Some recent simultaneous measurements of PAN and other atmospheric pollutants such as O_3, HNO_3,

TABLE 1-4. SUMMARY OF PARAMETERS USED IN DETERMINATION OF PAN BY GC-ECD

Reference	Column dimensions and material	Stationary phase	Solid support	Column temperature, °C	Flow rate, ml/min	Carrier gas	Elution time, min	Concentration range
Heuss and Glasson, 1968	4 ft x 1/8 in Glass	SE30 (3.8%)	80-100 Mesh Diatoporte S	25	N.A.[a]	N.A.[a]	N.A.[a]	ppb range
Grosjean, 1983	6 ft x 1/8 in Teflon	10% Carbowax 400	60/80 Mesh Chromosorb P	30	40	N_2	N.A.[a]	ppb range
Darley et al., 1963	3 ft x 1/9 in Glass	5% Carbowax 400	100-200 Mesh Chromosorb W	35	25	N_2	2.17	3 to 5 ppb
Stephens and Price, 1973	1.5 ft. x 1/8 in Teflon	5% Carbowax E 400	Chromosorb G 80/100 mesh treated with dimethyl dichlorosilane	25	60	N_2	1.75	37 ppb
Lonneman et al., 1976	3 to 4 ft x 1/8 in Glass	10% Carbowax 600	Gas Chrom Z	25	70	95% Ar 5% CH_4	2.7	0.1 to 100 ppb
Holdren and Spicer, 1984	5 ft x 1/8 in Teflon	60/80 Mesh Carbowax 600	Gas Chrom Z	35	70	90% Ar 10% CH_4	3.00	ppb
Peake and Sandhu, 1982	3.3 ft x 1/8 in Glass	5% Carbowax 600	Chromosorb W	33	50	N_2	N.A.[a]	0.2 to 20 ppb
Singh and Salas, 1983b	1.2 ft x 1/8 in Teflon	10% Carbowax 600	80/100 Mesh Supelcoport	33	30	95% AR 5% CH_4	N.A.[a]	0.02-0.10 ppb
Grosjean et al., 1984	1.7 ft x 1/8 in Teflon	10% Carbowax 400	60/80 Mesh Chromosorb G	30	40	N_2	5.0	2-400 ppb
Nielson et al., 1982	3.9 ft x 1/12 in Glass	5% Carbowax 400	Chromosorb W - AW - DCMS	25	40	N_2	6.0	11 ppb

[a] N.A. - not available in reference.

TABLE 1-5. INFRARED ABSORPTIVITIES OF PEROXYACETYL NITRATE

		Absorptivity, ppm^{-1} m^{-1} x 10^4				
Frequency cm^{-1}	Mode	Liquid PAN (Bruckmann and Willner, 1983)	PAN in air (Stephens, 1969)	Frequency cm^{-1}	PAN in air (Stephens and Price, 1973)	PAN in octane (Holdren and Spicer, 1984)
1842	$\nu(c{=}o)$	12.4	10.0	1830	10.0	9.44
1741	$\nu_{as}(NO_2)$	32.6	23.6	1728	23.6	26.5
1302	$\nu_s(NO_2)$	13.6	11.2	1294	11.4	9.44
1162.5	$\nu(c{-}o)$	15.8	14.3	1153	13.9	9.66
930	$\nu(o{-}o)$	N.A.[a]	N.A.[a]	930	1.8	N.A.[a]
791.5	$\delta(NO_2)$	13.4	10.1	787	10.3	10.1

[a] Not available in reference.

HCOOH, and HCHO have been made by long-path FTIR spectrometry during smog episodes in the Los Angeles Basin. Tuazon et al. (1978) describes an FTIR system operable at pathlengths up to 2 km for ambient measurements of PAN and other trace constituents. This system employed an eight-mirror multiple reflection cell with a 22.5-m base path. Detection of PAN was by bands at 793 and 1162 cm^{-1}. The 793 cm^{-1} band is characteristic of peroxynitrates, while the 1162 cm^{-1} band is reportedly attributable to PAN only (Hanst et al., 1982). Tuazon et al. (1981) reported a detection limit for PAN of 3 ppb at a 900-meter pathlength.

Hanst et al. (1982) made measurements with a 1260-m folded optical path system during a 2-day smog episode in Los Angeles in 1980. An upper limit of 1 ppb of peroxybenzoyl nitrate (PbzN) was placed, based on observations in the vicinity of the PBzN band at 990 cm^{-1}; the maximum PAN concentration observed was 15 ppb.

Sampling may constitute one of the major problems in the analysis of trace reactive species, such as PAN, by long-path FTIR spectrometry. The large internal surface area of the White cells may serve to promote the decomposition or irreversible adsorption of reactive trace species. High volume sampling rates and inert internal surface materials are used to minimize these effects.

Because of the thermal instability of dilute PAN samples and the explosive nature of purified PAN, calibration samples are not commercially available. Each laboratory involved in making such measurements must prepare its own standards. Calibration samples are usually prepared by various means at concentrations in the ppm range, and they must be analyzed by some absolute technique.

Earlier methods used to synthesize PAN have been summarized by Stephens (1969). The photolysis of alkyl nitrites in oxygen was the most commonly used procedure and may still be used by some investigators. As described by Stephens et al. (1965), the liquefied crude mixture obtained at the outlet of the photolysis chamber is purified by preparation-scale GC. [CAUTION: Both the liquid crude mixture and the purified PAN samples are violently explosive and should be handled behind explosion shields using plastic full-face protection, gloves, and a leather coat at all times.] The pure PAN is usually diluted to about 1000 ppm in nitrogen cylinders at 100 psig and stored at reduced temperatures, <15°C.

Gay et al. (1976) have used the photolysis of Cl_2:aldehyde:NO_2 mixtures in air or oxygen for the preparation of PAN and a number of its homologues at high yields. This procedure has been utilized in a portable PAN generator that can be used for the calibration of GC-ECD instruments in the field (Grosjean, 1983; Grosjean et al., 1984).

The other technique for PAN preparation in current use involves the nitration of peracetic acid. Several investigators have recently reported on a condensed-phase synthesis of PAN with peracetic acid that produces high yields of a pure product free of other alkyl nitrates (Hendry and Kenley, 1977; Kravetz et al., 1980; Nielsen et al., 1982; Holdren and Spicer, 1984). Most of these procedures call for the addition of peracetic acid (40 percent in acetic acid) to a hydrocarbon solvent (pentane, heptane, octane) maintained at 0°C in a dry-ice acetone bath, followed by acidification with sulfuric acid and slow addition of sodium nitrate. After the nitration is complete, the hydrocarbon fraction containing PAN concentrations of 2 to 4 mg/ml can be stored at -20°C for periods longer than a year (Holdren and Spicer, 1984).

The most direct method for absolute analysis of these PAN samples is by infrared absorption, using absorptivities given in Table 1-5. Conventional IR instruments and 10-cm gas cells can analyze gas standards of concentrations >35 ppm. Liquid microcells can be used for the analysis of PAN in octane solutions.

The alkaline hydrolysis of PAN to acetate ion and nitrite ion in quantitative yield (Nicksic et al., 1967) provides a means independent of infrared for the quantitative analysis of PAN. Following hydrolysis, nitrite ion may be quantitatively analyzed by the Saltzman colorimetric procedure (Stephens, 1969). The favored procedures now use ion chromatography to analyze for nitrite (Nielsen et al., 1982) or acetate (Grosjean, 1983, 1984) ions. Another calibration procedure has been proposed that is based on the thermal decomposition of PAN in the presence of excess NO (Lonneman et al., 1982). The peroxyradical, $CH_3C(O)O_2$, and its decomposition products rapidly oxidize NO to NO_2 with a stoichiometry that has been experimentally measured. By the use of NO standard mixtures and the measurement by chemiluminescence of the NO consumed, the absolute PAN concentration can be determined.

1.4.4.6 Methods for Sampling and Analysis of Hydrogen Peroxide. Hydrogen peroxide (H_2O_2), like ozone and PAN, is formed as a product of the photooxidation of hydrocarbons and reaches maximum concentrations during daylight hours. There are some early reports of H_2O_2 concentrations as high as 180 ppb at an ozone maximum of 650 ppb, but it now appears more likely that maximum H_2O_2 concentrations are in the range of 10 to 50 ppb and are only a small fraction (< 10%)

of the corresponding ozone maximum. Applied and potentially useful techniques for the measurement of ambient H_2O_2 are summarized in Table 1-6.

With the exception of Fourier-transform infrared (FTIR) studies, all of the techniques that have been used for atmospheric H_2O_2 measurements have employed aqueous traps for sampling. Recent studies have indicated that this approach leads to interference from ozone, which will always be present at higher concentrations. Absorbed O_3 has been observed to promote both the formation and destruction of H_2O_2 in aqueous media (Zika and Saltzman, 1982). Therefore, an obvious research need in H_2O_2 measurements is a clear delineation of the nature of any O_3 interferences and the development of means for their prevention.

Of the procedures given in Table 1-6, only the titanium colorimetric, enzyme-catalyzed, and FTIR methods have been used for atmospheric sampling. The other procedures do not appear promising for ambient air analysis. The titanium sulfate-8-quinolinol reagent has been used in several earlier studies on atmospheric H_2O_2 (Bufalini et al., 1972; Gay et al., 1972a; Gay et al., 1972b; Kok et al., 1978a). Hydrogen peroxide in air is scrubbed in a coarse-fritted bubbler containing aqueous titanium sulfate-ammonium sulfate-sulfuric acid solution. After sampling, the solution is extracted with an aliquot of 8-quinolinol in chloroform. The absorbance at 450 nm of the titanium (IV)-H_2O_2-9-quinolinol complex in chloroform is determined. A positive interference is expected from any compound that can liberate H_2O_2 via acid hydrolysis (Pobiner, 1961), e.g., t-butylhydroperoxide. Of the major atmospheric pollutants investigated (SO_2, O_3, NO_2, NO, and hydrocarbons), only SO_2 at high concentrations gave a small (0.7 percent) negative interference (Gay et al., 1972b).

In the titanium tetrachloride method, samples are collected in a midget impinger containing an aqueous $TiCl_4$-HCl solution. A stable $TiCl_4$-H_2O_2 complex is formed immediately, and after the solution is diluted to a known volume, the absorbance of the complex at 410 nm is determined. The principal difficulty with this method is the formation of fine particles, presumably TiO_2, which scatter visible radiation and create an apparent absorption. In an intercomparison of H_2O_2 measurement methods, Kok et al. (1978a) reported rather poor agreement between the two titanium reagents and between these and chemiluminescence.

A promising method for the measurement of hydrogen peroxide in the atmosphere at very low concentrations is based on the chemiluminescence obtained from the Cu(II)-catalyzed oxidation of luminol (5-amino-2,3 dihydro-1,4-phthalazinedione) by H_2O_2 (Armstrong and Humphreys, 1965). The product of the reaction with

TABLE 1-6. MEASUREMENT METHODS FOR HYDROGEN PEROXIDE

Method	Reagent(s)	Limits of detection[a]	Interferences[b]		Applications	Primary reference
			Positive	Negative		
Titanium colorimetry	(1) Titanium Sulfate -8-Quinolinol (2) Titanium Tetrachloride	(1) 1.6×10^{-6} M (2) ca 10^{-6} M	Alkyl hydroperoxides	SO_2[c]?	Atmospheric	(1) Gay et al. (1972a, 1972b) (2) Pilz and Johann (1974); Kok et al. (1978a)
Chemiluminescence	Luminol, Cu(II) basic solution	0.001 to 1 ppm	PAN[d]	SO_2[e]	Atmospheric, rainwater	Armstrong and Humphreys (1965); Kok et al. (1978a,1978b)
Enzyme-catalyzed	Scopoletin, horseradish-peroxidase (HRP)	1.5×10^{-11} M	NA	NA	Atmospheric, rainwater	Andreae (1955); Perschke and Broda (1961); Zika and Saltzman (1982)
Enzyme-catalyzed	Leuco crystal violet, HRP	10^{-8} M	NA	NA	---	Mottola et al. (1970)
Enzyme-catalyzed	3-(p-hydroxyphenyl) propionic acid	10^{-6} to 10^{-4} M[f]	NA	NA	---	Zaitsu and Ohkura (1980)
Fourier-transform infrared absorption	None	0.005 ppm (est.)	NA[g]	None	Atmospheric[h]	Hanst et al. (1982)
Electrochemical	Aqueous solutions	5×10^{-6} to 1 M	NA	NA	---	Pisarevskii and Polozova (1980)
H_2O_2-olefin reactions	1,2-di-(4-pyridyl) ethylene	10^{-6} to 5×10^{-4} M	O_3	NA	---	Hauser and Kolar (1968)
Mixed-ligand complex reagents	Vanadium and uranium hydroxamic acid chelates	10^{-6} M	NA	NA	---	Csanyi (1981); Meloan et al. (1961)

[a] Except where noted, detection limits are in moles/liter(M) in aqueous solution.

[b] O_3 may be both a positive and negative interference in all these procedures using aqueous sampling. See Text. NA = not available.

[c] The SO_2 interferences is reported to be small at high SO_2 concentrations (Gay et al., 1972b). Studies of potential positive and negative interferences are incomplete for these methods.

[d] The reported PAN interference is small (Kok et al., 1978b).

[e] The report of an SO_2 interference is undocumented.

[f] The lower limit could presumably be reduced by the use of larger samples.

[g] With sufficient resolution, there should be no interferences. IR absorption by atmospheric water vapor is the major analytical limitation.

[h] H_2O_2 bands have not been observed in any long-path FTIR studies. The estimated lower limit of detection in these studies is approximately 0.005 ppm.

H_2O_2 is 3-amino-phthalic acid, a nitrogen molecule, and a photon of light at 450 nm. A small positive interference was reported for PAN (Kok et al., 1978b). If O_3 absorption leads to the formation of H_2O_2 as reported (Zika and Saltzman, 1982; Heikes et al., 1982), then O_3 is a major interference. There have also been undocumented reports of a negative interference from SO_2.

Perhaps the most promising chemical approach for the measurement of trace concentrations of H_2O_2 employs the catalytic acitivity of the enzyme, horseradish peroxidase (HRP), on the oxidation of organic substrates by H_2O_2. This general method involves three components: a substrate that is oxidizable, HRP, and H_2O_2. Three substrates that have been used are scopoletin (6-methoxy-7-hydroxy-1,2-benzopyrone), 3-(p-hydroxyphenyl)propionic acid (HPPA), and leuco crystal violet (LCV). The scopoletin reagent has recently been used in atmospheric analysis. The disappearance of scopoletin fluorescence, upon oxidation of scopoletin by H_2O_2, is monitored and the fluorescence intensity is used to obtain the concentration of H_2O_2 from a calibration curve. The most significant advantage of the scopoletin method is the sensitivity (ca. 16^{-11} M). The chief disadvantage of the method is that the concentration of H_2O_2 must be within a narrow concentration range in order to obtain an accurately measurable decrease in fluorescence. This limits the usefulness of the technique in determining unknown H_2O_2 concentrations over several orders of magnitude. With the leuco crystal violet (LCV) substrate, intensely colored crystal violet is formed from the reaction of H_2O_2 with LCV, catalyzed by HRP. The absorbance is measured at 596 nm, where the molar absorption coefficient of crystal violet is 10^5 M^{-1} cm^{-1}, a very high value and an inherent advantage of this method. Finally, Zaitsu and Ohkura (1980) have tested a number of 4-hydroxy phenyl compounds and found that 3-(p-hydroxyphenyl) propionic acid (HPPA) provided a sensitive and rapid means for determining H_2O_2. A product is formed that fluoresces at 404 nm, and the intensity of this fluorescence is monitored as a function of H_2O_2 concentration. The detection limit was reported to be 10^{-10} mole H_2O_2 with a test solution of only 0.1 ml volume used. The molar sensitivity could presumably be improved by the use of large sample volumes.

The enzymatic methods appear to be the most promising colorimetric methods of H_2O_2 and have considerably greater sensitivity than the methods employing titanium reagents. However, studies of potential atmospheric interferences have apparently not been conducted for any of these three substrates.

Hydrogen peroxide can be monitored directly in the gas phase by FTIR absorption at 1250 cm^{-1}, where the absorption coefficient is 8.4 cm^{-1} atm^{-1} at 1 cm resolution (Hanst et al., 1981). One FTIR measurement of the possible presence of 0.070 ppm H_2O_2 was reported during an intense smog episode in Pasadena, California (Hanst et al., 1975). Unfortunately, minimum detection limits at 1 km pathlength are degraded to 0.040 ppm because of neighboring absorption bands of H_2O and CH_4 (Hanst et al., 1981).

As with O_3, H_2O_2 calibration standards are not commercially available and are usually prepared at the time of use. The most convenient method for preparing aqueous samples containing micromolar concentrations of H_2O_2 is simply the serial dilution of commerical grade 30 percent H_2O_2 (Fisher Analytical Reagent). Techniques for the convenient generation of gas-phase standards are not available. A technique often used for generating ppm concentrations of H_2O_2 in air involves the injection of microliter quantities of 30 percent H_2O_2 solution into a metered stream of air that flows into a Teflon bag. Aqueous and gas-phase samples are then standardized by conventional iodometric procedures (Allen et al., 1952; Cohen et al., 1967).

Hydrogen peroxide liberates iodine from an iodide solution quite slowly, but in the presence of a molybdate catalyst the reaction is rapid. The iodine liberated can be determined by titration with standard thiosulfate at higher concentrations or by photometric measurement of the tri-iodide ion at low concentrations. The molar absorption coefficient of the tri-iodide ion at 350 nm has been determined to be 2.44×10^4 (Armstrong and Humphreys, 1965). The stoichiometry is apparently 1 mole of iodine released per mole of H_2O_2. However, definitive studies of the stoichiometry have not been performed for H_2O_2 as they have for the iodometric determination of O_3.

1.5 CONCENTRATIONS OF OZONE AND OTHER PHOTOCHEMICAL OXIDANTS IN AMBIENT AIR

In the context of this document, the concentrations of ozone and other photochemical oxidants found in ambient air are important for:

1. Assessing potential exposure of individuals; communities; the general population and those subpopulations in communities that may be especially susceptible to adverse effects from these oxidants; natural ecosystems, managed ecosystems such as crops; and nonbiological materials such as polymers and paints.

2. Assessing whether levels of ozone and other photochemical oxidants in ambient air are within or near the range of concentrations shown to produce adverse effects in health and welfare effects studies.

3. Determining whether levels of ozone and other photochemical oxidants are as high indoors as in the ambient air, for the purpose of assessing actual, as opposed to potential, exposures of individuals in the general population or susceptible subpopulations.

4. Assessing whether non-ozone photochemical oxidants occur in ambient air at levels within or near the range of concentrations shown to produce potentially adverse effects in health and welfare effects studies.

5. Assessing whether concentrations of ozone plus the other photochemical oxidants together occur at levels sufficient to produce adverse effects in the general or susceptible subpopulations, or in vegetation and ecosystems.

6. Evaluating the relationship(s) between ozone and the other photochemical oxidants, in order to determine whether ozone can function as a control surrogate in the event that these other, non-ozone photochemical oxidants are found to produce adverse effects on public health and welfare.

1.5.1 Ozone Concentrations in Urban Areas

The current ozone standard is expressed in terms of a 1-hour value not to be exceeded on more than 1 day per year. Thus, the second-highest value is a concentration of significance, since it determines compliance with the standard and is, thereby, an indicator of exposures having potential health and welfare significance.

In Chapter 6, the second-highest 1-hour ozone concentrations reported in each of 4 years have been given for the 80 most populous Standard Metropolitan Statistical Areas (SMSAs) of the United States, i.e., those with populations $\geq$ 0.5 million. In Table 1-7, 1982 ozone concentrations for the subset of SMSAs with populations $\geq$ 1 million are given by geographic area, demarcated according to United States Census divisions and regions (U.S. Department of Commerce, 1982). The second-highest concentrations measured in 1982 in those 38 SMSAs having populations of at least 1 million ranged from 0.09 ppm in the Ft. Lauderdale, Florida, and Seattle, Washington, areas to 0.32 ppm in the Los Angeles and Riverside, California, areas. The second-highest 1-hour ozone concentrations for 32 of the 38 SMSAs in Table 1-7 equal or exceed 0.12 ppm. The data clearly show, as well, that the highest 1-hour ozone concentrations in the United States occur in the northeast (New England and Middle Atlantic

TABLE 1-7. SECOND-HIGHEST 1-HR OZONE CONCENTRATIONS IN 1982 IN STANDARD METROPOLITAN STATISTICAL AREAS WITH POPULATIONS ≥ 1 MILLION, GIVEN BY CENSUS DIVISIONS AND REGIONS[a]

Division and region	SMSA	SMSA population, millions	Second-highest 1982 O_3 concn., ppm
NORTHEAST			
New England	Boston, MA	>2	0.16
Middle Atlantic	Buffalo, NY	1 to <2	0.11
	Nassau-Suffolk, NY	>2	0.13
	Newark, NJ	1 to <2	0.17
	New York, NY/NJ	>2	0.17
	Philadelphia, PA/NJ	>2	0.18
	Pittsburgh, PA	>2	0.14
SOUTH			
South Atlantic	Atlanta, GA	>2	0.14
	Baltimore, MD	>2	0.14
	Ft. Lauderdale-Hollywood, FL	1 to <2	0.09
	Miami, FL	1 to <2	0.14
	Tampa-St. Petersburg, FL	1 to <2	0.11
	Washington, DC/MD/VA	>2	0.15
SOUTH			
West South Central	Dallas-Ft. Worth, TX	>2	0.17
	Houston, TX	>2	0.21
	New Orleans, LA	1 to <2	0.17
	San Antonio, TX	1 to <2	0.14
NORTH CENTRAL			
East North Central	Chicago, IL	>2	0.12
	Detroit, MI	>2	0.16
	Cleveland, OH	1 to <2	0.12
	Cincinnati, OH/KY/IN	1 to <2	0.13
	Milwaukee, WI	1 to <2	0.13
	Indianapolis, IN	1 to <2	0.12
	Columbus, OH	1 to <2	0.13
West North Central	St. Louis, MO/IL	>2	0.15
	Minneapolis-St. Paul, MN/WI	>2	0.10
	Kansas City, MO/KS	1 to <2	0.10

TABLE 1-7 (cont'd). SECOND-HIGHEST 1-HR OZONE CONCENTRATIONS IN 1982 IN STANDARD METROPOLITAN STATISTICAL AREAS WITH POPULATIONS $\geq$ 1 MILLION GIVEN BY CENSUS DIVISIONS AND REGIONS[a]

Division and region	SMSA	SMSA population, millions	Second-highest 1982 O_3 concn., ppm
WEST			
Mountain	Denver-Boulder, CO	1 to <2	0.14
	Phoenix, AZ	1 to <2	0.12
Pacific	Los Angeles-Long Beach, CA	>2	0.32
	San Francisco-Oakland, CA	>2	0.14
	Anaheim-Santa Ana-Garden Grove, CA	1 to <2	0.18
	San Diego, CA	1 to <2	0.21
	Seattle-Everett, WA	1 to <2	0.09
	Riverside-San Bernardino-Ontario, CA	1 to <2	0.32
	San Jose, CA	1 to <2	0.14
	Portland, OR/WA	1 to <2	0.12
	Sacramento, CA	1 to <2	0.16

[a] Standard Metropolitan Statistical Areas and geographic divisions and regions as defined by Statistical Abstract of the United States (U.S. Department of Commerce, 1982).

Source: U.S. Environmental Protection Agency, SAROAD data file for 1982.

States), in the Gulf Coast area (West South Central states), and on the west coast (Pacific states). Second-highest 1-hour concentrations in the SMSAs within each of these three areas averaged 0.15, 0.17, and 0.19 ppm, respectively, for 1982. It should be emphasized that these three areas of the United States are subject to those meteorological and climatological factors that are conducive to local oxidant formation, or transport, or both. It should also be emphasized that 11 of the 16 SMSAs in the country with populations $\geq$ 2 million are located in these areas.

Sources of oxidant precursors are strongly correlated with population (Chapter 3). In accord with this relationship, three population groups within the 80 largest SMSAs had the following median values for their collective second-highest 1-hour ozone concentrations in both 1981 and 1982: populations $\geq$ 2 million, 0.15 ppm O_3; populations of 1 to 2 million, 0.13 ppm O_3; and populations of 0.5 to 1 million, 0.12 ppm O_3.

Among all stations reporting valid ozone data ($\geq$ 75 percent of possible hourly values per year) in 1979, 1980, and 1981 (collectively, 906 station-years) in the United States, the median second-highest 1-hour ozone value was 0.12 ppm, and 5 percent of these stations reported second-highest 1-hour values $\geq$ 0.28 ppm (Figure 1-3).

A pattern of concern in assessing human physiological and vegetational responses to ozone is the occurrence of repeated or prolonged periods, or both, when the ozone concentrations equal or exceed levels near those known to elicit responses. In addition, the number of days of respite between such multiple-day periods of high ozone is of possible consequence. Data presented in Chapter 6 show that the probabilities of prolonged exposures to (consecutive days) or respites from (consecutive days) specified concentrations are location-specific. In Pasadena, CA, a high-ozone area, there is a 42 percent probability (based on 1979 through 1981 aerometric data) that an ozone concentration of 0.18 ppm, once reached, is likely to persist for 3 days or longer. Other, lower-ozone areas show lower probabilities of such multiday high ozone concentrations. These and other data presented demonstrate the occurrence, at least in some urban areas, of multiple-day exposures to relatively high concentrations of ozone.

1.5.2. Trends in Urban and Nationwide Ozone Concentrations

Discussion in Chapter 5 pointed out and substantiated that aerometric data obtained by potassium iodide methods in earlier years are essentially concentrations of ozone rather than "total oxidants." Comparison of concentrations of "total oxidants" in major urban areas for 1974 and 1975 (U.S. Environmental Protection Agency, 1978) with ozone data for those same urban areas for 1979 through 1982 (U.S. Environmental Protection Agency, SAROAD file) shows that the more recent ozone concentrations are in the same general range for many cities, have declined in some, and are somewhat higher in others.

Trends in nationwide ozone concentrations, gauged by annual averages at two subsets of stations reporting data from 1974 through 1981, show declines of 15 to 20 percent. These trend data represent urban areas almost exclusively. Interpretation of this trend is complicated by four potentially significant influences: (1) a change in calibration procedure (1979); (2) improved data-quality audits (1979); (3) possible shifts in underlying meteorological patterns;

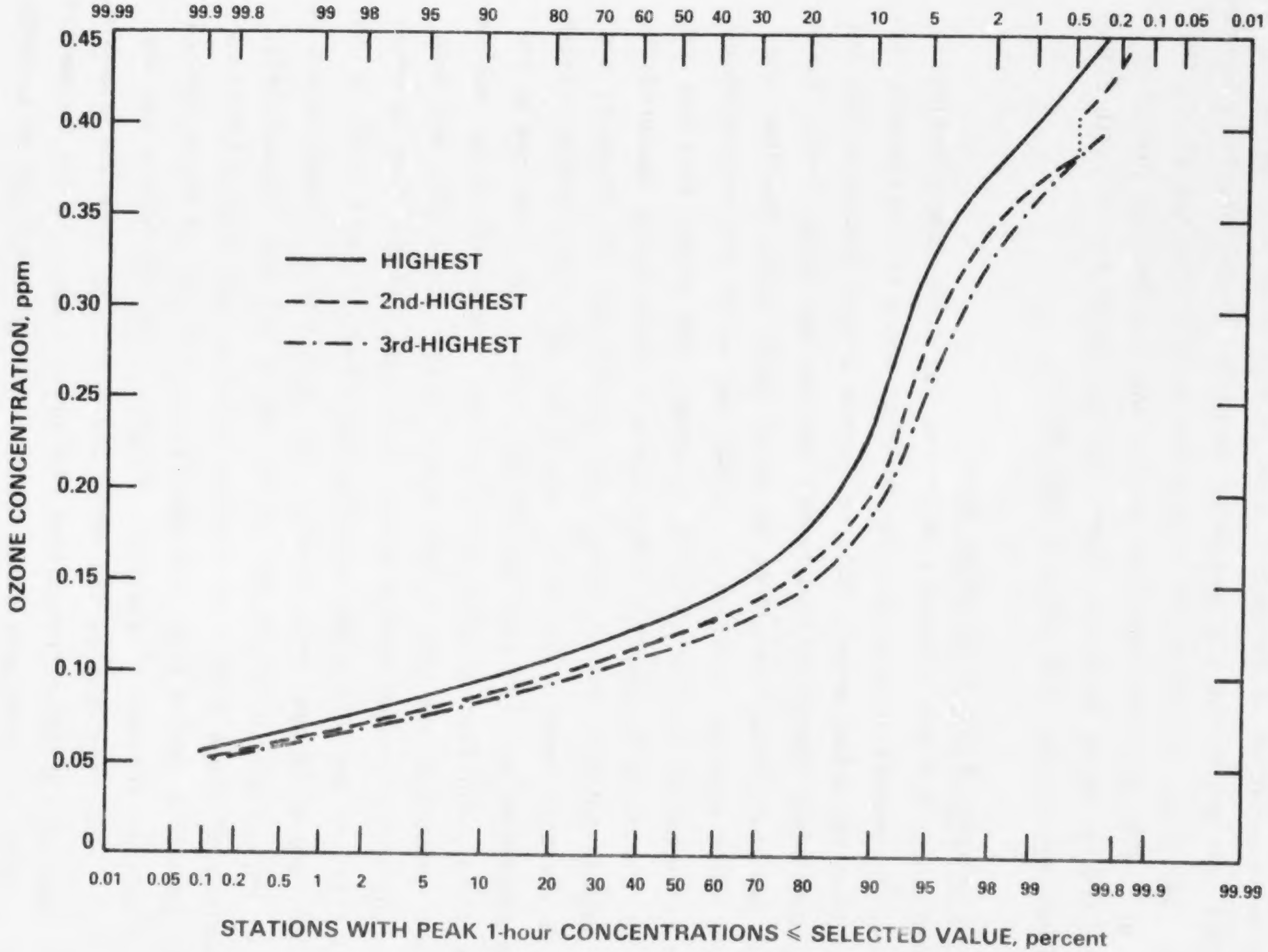

Figure 1-3. Collective distributions of the three highest 1-hour ozone concentrations for 3 years (1979, 1980, and 1981) at valid sites (906 station-years).

and (4) changes in precursor emission rates. When adjustments for the first two factors are made, a portion of the decrease is real. The exact portion of the decline that is attributable to the calibration change can not be determined without minute examination of aerometric data records from each monitoring station, since some monitoring stations began using the UV calibration procedure as early as 1975, some changed to UV calibration in 1979 (but not all in the same month of 1979), and some used the interim BAKI calibration procedure permitted by EPA for up to 18 months after promulgation of the UV calibration procedure (Hunt and Curran, 1982; also Chapter 5).

1.5.3. Ozone Concentrations in Nonurban Areas

Nonurban areas are not routinely monitored for ozone concentrations. Consequently, the aerometric data base for nonurban areas is considerably less substantial than for urban areas. Data on maximum 1-hour concentrations and arithmetic mean 1-hour concentrations reveal that maximum (peak) 1-hour concentrations at nonurban sites classified as rural (SURE study, Martinez and Singh, 1979; NAPBN studies, Evans et al., 1982) may exceed the concentrations observed at nonurban sites classified as suburban (SURE study, Martinez and Singh, 1979). For example, maximum 1-hour ozone concentrations measured in 1980 at Kisatchie National Forest (NF), Louisiana; Custer NF, Montana; and Green Mt. NF, Vermont, were 0.105, 0.070, and 0.115 ppm, respectively. Arithmetic mean concentrations for 1980 were 0.028, 0.037, and 0.032 ppm at the respective sites. For four nonurban (rural) sites in the SURE study, maximum 1-hour ozone concentrations were 0.106, 0.107, 0.117, and 0.153; and mean 1-hour concentrations ranged from 0.021 to 0.035 ppm. At the five nonurban (suburban) sites of the SURE study, maximum concentrations were 0.077, 0.099, 0.099, 0.080, and 0.118 ppm, respectively. The mean 1-hour concentrations at those sites were 0.023, 0.030, 0.025, 0.020, and 0.025 ppm, respectively.

Comparison of these data with data for nonurban and remote locations during the 1973-1976 period show that mean concentrations at these various nonurban locations are not dissimilar. Ranges of concentrations and the maximum 1-hour concentrations at the NAPBN and SURE sites show the probable influence, however, of ozone transported from urban areas. In one documented case, for example, a 1-hour peak ozone concentration of 0.125 ppm at an NAPBN site in Mark Twain National Forest, Missouri, was measured during passage of an air mass whose trajectory was calculated to have included Detroit, Cincinnati, and Louisville in the preceding hours (Evans et al., 1982).

These data corroborate the conclusion given in the 1978 criteria document (U.S. Environmental Protection Agency, 1978) regarding urban-nonurban and urban-suburban gradients; i.e., nonurban areas may sustain higher ozone concentrations than those found in urban areas. Reasons for this phenomenon include induction and transport times, as well as the possible additive effects of plumes from suburban or smaller areas as air masses pass over them downwind from urban areas. Generally, however, lower ozone concentrations occur in nonurban areas, as the data in Chapter 6 indicate.

1.5.4. Patterns in Ozone Concentrations

Since the photochemical reactions of precursors that result in ozone formation are driven by sunlight, as well as emissions, the patterns of ozone occurrence in ambient air depend on daily and seasonal variations in sunlight intensity. The typical diurnal pattern of ozone in ambient air has a minimum ozone level around sunrise (near zero in most urban areas), increasing through the morning to a peak concentration in early afternoon, and decreasing toward minimal levels again in the evening. Obviously, meteorology is a controlling factor; if strong winds disperse the precursors or heavy clouds intercept the sunlight, high ozone levels will not develop. Another important variation in the basic diurnal pattern appears in some localities as a secondary peak in addition to the early afternoon peak. This secondary peak may occur any time from midafternoon to the middle of the night and is attributed to ozone transported from an upwind area where high ozone levels have occurred earlier in the day. As documented in Chapter 6, secondary peak concentrations may be higher than concentrations resulting from the photochemical reactions of locally emitted precursors (Martinez and Singh, 1979). At one nonurban site in Massachusetts, for example, primary peak concentrations of about 0.11, 0.14, and 0.14 occurred at noon, from noon to about 4:00 p.m., and at noon, respectively, on 3 successive days of high ozone levels (Martinez and Singh, 1979). Secondary peaks at the same site for those same 3 days were about 0.150, 0.157, and 0.130 ppm at about 6:00 p.m., 8:00 p.m., and 8:00 p.m., respectively (Martinez and Singh, 1979).

Because weather patterns, ambient temperatures, and the intensity and wavelengths of sunlight all play important roles in oxidant formation, strong seasonal as well as diurnal patterns exist. The highest ozone levels occur in the summer and fall (second and third quarters), when sunlight reaching the lower troposphere is most intense and stagnant meteorological conditions augment the potential for ozone formation and accumulation. Average summer afternoon levels can be from 150 to 250 percent of the average winter afternoon levels. Minor variations in the smog season occur with location, however. In addition, it is possible for the maximum and second-highest 1-hour ozone concentrations to occur outside the two quarters of highest average ozone concentrations (cf. data for Tucson, Arizona, and data for the California sites given in Chapter 6). Exceptions to seasonal patterns are important considerations with regard to the protection of crops from ozone damage, especially since respective crops have different growing seasons in terms of length, time of year, and areas of the country in which they are grown.

As data for different averaging times clearly demonstrate, averaging smooths out and submerges the occurrence of peak concentrations. This is an obvious and familiar statistical phenomenon. It is pointed out, however, because it has direct relevance to the protection of public health and welfare. Averaging times must correspond to or be related in a consistent manner to the pattern of exposure that elicits untoward responses.

Certain spatial variations in ozone concentrations occur that are generally of little consequence in exposure assessment. For example, ozone concentrations increase with increasing altitude (e.g., Viezee and Singh, 1981). The gradients are of no known consequence for inhabited elevations. They could potentially be of some consequence for high-altitude flights unless compensated for by adequate ventilation/filtration systems. Likewise, ozone concentrations exhibit hemispheric asymmetry (Logan et al., 1981), with concentrations highest in the northern hemisphere. Aerometric data sufficiently describe concentrations in the latitudes of the United States such that the fact of asymmetry has no practical consequences.

Spatial variations on a smaller scale assume more importance relative to exposure assessment. Indoor-outdoor gradients in ozone concentrations are known to occur even in structures ventilated by fresh air rather than air conditioning (e.g., Sabersky et al., 1973; Thompson et al., 1973). Ozone reacts with surfaces inside buildings, so that decay occurs fairly rapidly. Ratios of indoor-to-outdoor (I/O) ozone concentrations are quite variable, however, since the presence or absence of air conditioning, air infiltration or exchange rates, interior air circulation rates, and the composition of interior surfaces all affect indoor ozone concentrations. Ratios (I/O) in the literature thus vary from 80 ± 10 percent (Sabersky et al., 1973) in an air-conditioned office building (but with 100 percent outside air intake) to 10 to 25 percent in air-conditioned residences (Berk et al., 1981).

On a larger scale, within-city variations in ozone concentrations can occur, despite the commonly accepted maxim that ozone is a regional pollutant. Data in Chapter 6 show, for example, relatively homogeneous ozone concentrations in New Haven, Connecticut (U.S. Environmental Protection Agency, SAROAD files), which is a moderately large city downwind of a reasonably well-mixed urban plume (Cleveland et al., 1976). In a large metropolis such as New York City, however, appreciable gradients in ozone concentration can exist from one side of the city to the other (Smith, 1981). Such gradients must be taken into consideration in exposure assessments.

1.5.5 Concentrations and Patterns of Other Photochemical Oxidants

1.5.5.1 Concentrations. No aerometric data are routinely obtained by Federal, state, or local air pollution agencies for any photochemical oxidants other than nitrogen dioxide and ozone. The concentrations presented in Chapter 6 for non-ozone oxidants were all obtained in special field investigations. The limitations in the number of locations and areas of the country represented in the information presented simply reflect the relative paucity of data in the published literature.

The four non-ozone photochemical oxidants for which concentration data have been presented are formic acid, peroxyacetyl nitrate (PAN), peroxypropionyl nitrate (PPN), and hydrogen peroxide. Peroxybenzoylnitrate has not been clearly identified in ambient air in the United States.

Recent data indicate the presence in urban atmospheres of only trace amounts of formic acid ($\leq$ 15 ppb, measured by FTIR). Estimates in the earlier literature (1950s) of 600 to 700 ppb of formic acid in smoggy atmospheres were erroneous because of faulty measurement methodology (Hanst et al., 1982).

The measurement methods (IR and GC-ECD) for PAN and PPN are specific and highly sensitive, and have been in use in air pollution research for nearly two decades. Thus, the more recent literature on the concentrations of PAN and PPN confirm and extend, but do not contradict, earlier findings reported in the two previous criteria documents for ozone and other photochemical oxidants (U.S. Department of Health, Education, and Welfare, 1970; U.S. Environmental Protection Agency, 1978).

Concentrations of PAN have been reported in the air pollution literature from about 1960 through the present. The highest concentrations reported over this extended period were those found in the 1960s in the Los Angeles area: 70 ppb (1960), 214 ppb (1965); and 68 ppb (1968) (Renzetti and Bryan, 1961; Mayrsohn and Brooks, 1965; Lonneman et al., 1976; respectively).

The highest concentrations of PAN measured and reported in the past 5 years were 42 ppb at Riverside, California, in 1980 (Temple and Taylor, 1983), and 47 ppb at Claremont, California, also in 1980 (Grosjean, 1981). These are clearly the maximum concentrations of PAN reported for California and for the entire country in this period. Other recently measured PAN concentrations in the Los Angeles Basin were in the range of 10 to 20 ppb. Average concentrations of PAN in the Los Angeles Basin in the past 5 years ranged from 4 to 13 ppb (Tuazon et al., 1981a; Grosjean, 1981; respectively). Only one published report covering PAN concentrations outside California in the past 5 years is that of Lewis et al. (1983) for New Brunswick, New Jersey. The average PAN concentration was 0.5 ppb and the maximum was 11 ppb during a study done there from September 1978 through May 1980. Studies outside California from the early 1970s through 1978 showed average PAN concentrations ranging from 0.4 ppb in Houston, Texas, in 1976 (Westberg et al., 1978) to 6.3 ppb in St. Louis, Missouri, in 1973 (Lonneman et al., 1976). Maximum PAN concentrations outside California for the same period ranged from 10 ppb in Dayton, Ohio, in 1974 (Spicer et al., 1976) to 25 ppb in St. Louis (Lonneman et al., 1976).

Reports of PPN concentrations appear in the literature from about 1963 through the present. The highest PPN concentration reported in early studies was 6 ppb in Riverside, California (Darley et al., 1963). The next highest reported PPN concentration was 5 ppb at St. Louis, Missouri, in 1973 (Lonneman et al., 1976). Among more recent data, maximum PPN concentrations at respective sites ranged from 0.07 ppb in Pittsburgh, Pennsylvania, in 1981 (Singh et al.,

1982) to 3.1 ppb at Staten Island, New York (Singh et al., 1982). California concentrations fell within this range. Average PPN concentrations at the respective sites for the more recent data ranged from 0.05 ppb at Denver and Pittsburgh to 0.7 ppb at Los Angeles in 1979 (Singh et al., 1981).

Altshuller (1983) has succinctly summarized the nonurban concentrations of PAN and PPN by pointing out that they overlap the lower end of the range of urban concentrations at sites outside California. At remote locations, PAN and PPN concentrations are lower than even the lowest of the urban concentrations (by a factor of 3 to 4).

In urban areas, hydrogen peroxide (H_2O_2) concentrations have been reported to range from $\leq$ 0.5 ppb in Boulder, Colorado (Heikes et al., 1982) to $\leq$ 180 ppb in Riverside, California (Bufalini et al., 1972). In nonurban areas, reported concentrations ranged from 0.2 ppb near Boulder, Colorado, in 1978 (Kelly et al., 1979) to $\leq$ 7 ppb 54 km southeast of Tucson, Arizona (Farmer and Dawson, 1982). These nonurban data were obtained by the luminol chemiluminescence technique (see Chapter 5). The urban data were obtained by a variety of methods, including the luminol chemiluminescence, the titanium (IV) sulfate 8-quinolinol, and other wet chemical methods (see Chapter 5).

The higher concentrations of H_2O_2 reported in the literature must be regarded as especially problematic, since FTIR measurements of ambient air have not demonstrated unequivocally the presence of H_2O_2 even in the high-oxidant atmosphere of the Los Angeles area. The limit of detection for a 1-km-pathlength FTIR system is around 0.04 ppm (Chapter 5); FTIR is capable of measuring concentrations of H_2O_2 if it is present above the limit of detection.

1.5.5.2 Patterns. The patterns of formic acid (HCOOH), PAN, PPN, and H_2O_2 may be summarized fairly succinctly. They bear qualitative but not quantitative resemblance to the patterns already summarized for ozone concentrations. Qualitatively, diurnal patterns are similar, with peak concentrations of each of these occurring in close proximity to the time of the ozone peak. The correspondence in time of day is not exact, but is close. As the work of Tuazon et al. (1981) at Claremont, California, demonstrates, ozone concentrations return to baseline levels faster than the concentrations of PAN, HCOOH, or H_2O_2 (PPN was not measured). The diurnal patterns of PAN were reported in earlier criteria documents. Newer data merely confirm those patterns.

Seasonally, winter concentrations (third and fourth quarters) of PAN are lower than summer concentrations (second and third quarters). The winter concentrations of PAN are proportionally higher, however, than the winter concentrations of ozone; i.e., PAN-to-ozone ratios are higher in winter. Data are not readily available on the seasonal patterns of the other non-ozone oxidants.

Indoor-outdoor data on PAN are limited to one report (Thompson et al., 1973), which confirms the pattern to be expected from the known chemistry of PAN; that is, it persists longer indoors than ozone. Data are lacking for the other non-ozone oxidants.

1.5.6 Relationship Between Ozone and Other Photochemical Oxidants

The relationship between ozone concentrations and the concentrations of PAN, PPN, H_2O_2, and HCOOH is important only if these non-ozone oxidants are shown to produce adverse health or welfare effects, singly, in combination with each other, or in various combinations with ozone. If only ozone is shown to produce adverse health or welfare effects, then only ozone needs to be controlled. If any or all these other four oxidants is shown to produce adverse health or welfare effects, then it, or they, will also have to be controlled. Since ozone and all four of the other oxidants arise from reactions among the same organic and inorganic precursors, an obvious question is whether the control of ozone will also result in the control of the other four oxidants.

Chapters 7 through 9 of this report document what is known about the welfare effects of PAN (see Sections 1.6 through 1.8). No data are available regarding the possible welfare effects of HCOOH, H_2O_2, or PPN. Chapters 10 through 13 document what is known about the health effects of PAN and H_2O_2 (see Sections 1.10 through 1.13). Formic acid is not covered because of extremely limited aerometric data and no health effects data pertinent to the trace quantities of formic acid measured in the ambient air. No health effects data are available for PPN. One report that PBzN is a potent lachrymator is not discussed in the health effects chapters since no reliable data indicate its presence in ambient air, even in high-oxidant areas. The health effects data reported in Chapter 10 on H_2O_2 show that all levels tested to date are orders of magnitude above even the highest concentrations reported for ambient air; and, as noted above, the highest concentrations reported for ambient air are not strongly documented. Thus, the brief discussion below focuses on the relationship between ozone and PAN concentrations in ambient air.

The most straightforward evidence of the lack of a quantitative, monotonic relationship between ozone and the other photochemical oxidants is the range of PAN-to-O_3 and, indirectly, of PAN-to-PPN ratios presented in the review of Altshuller (1983) and summarized in Chapter 6. Ratios of PAN concentrations to ozone concentrations, as derived by Altshuller (1983), show that PAN-to-peak O_3 ratios vary from 1 to 12 across the country (PAN at time of O_3 peak); ratios for average PAN to average O_3 concentrations vary from 2 to 20 across the country. The correspondence between PAN and ozone concentrations is not exact but is similar for most locations at which both pollutants have been measured concurrently. Disparities between locations point up the lack of a consistent quantitative relationship. Likewise, disparities between the ratio of the average concentrations of the two pollutants and the ratio of their concentrations when ozone is at its maximum level also point up the lack of a monotonically quantitative relationship.

Certain other information presented in this chapter bears out the lack of a monotonic relationship between ozone and PAN. Not only are ozone-PAN relationships not consistent between different urban areas, but they are not consistent in urban versus nonurban areas, in summer versus winter, in indoor versus outdoor environments, or even, as the ratio data show, in location, timing, or magnitude of diurnal peak concentrations within the same city. Data obtained in Houston by Jorgen et al. (1978) show variations in peak concentrations of PAN measured concurrently at three separate monitoring sites in the same city. Temple and Taylor (1983) have shown that PAN concentrations are a greater percentage of ozone concentrations in winter than in the remainder of the year in California. Lonneman et al. (1976) demonstrated that PAN-to-O3 ratios are considerably lower in nonurban than in urban areas. Thompson et al. (1973) showed that PAN persists longer than ozone indoors. (This is to be expected from its lower reactivity with surfaces and its enhanced stability at cooler-than-ambient temperatures such as found in air-conditioned buildings.) Tuazon et al. (1981b) demonstrated that PAN persists in ambient air longer than ozone, its persistence paralleling that of nitric acid, at least in the locality studied (Claremont, CA). Reactivity data presented in the 1978 criteria document for ozone and other photochemical oxidants indicated that all precursors that give rise to PAN also give rise to ozone. The data also showed, however, that not all precursors giving rise to ozone also give rise to PAN. Not all that give rise to both are equally reactive toward both, however; and therefore some precursors preferentially give rise, on the basis of units of product per unit of reactant, to more of one product than the other (U.S. Environmental Protection Agency, 1978).

Altshuller (1983) prepared for the U.S. Environmental Protection Agency a comprehensive review and analysis of concentrations and relationships for ozone and other smog components, including PAN. The smog components he reviewed relative to ozone included aldehydes, aerosols, and nitric acid, as well as the non-ozone oxidants covered in this chapter. It must be emphasized that Altshuller examined the issue of whether ozone could serve as an abatement surrogate for all photochemical products, not just oxidants and not just the subset of photochemical oxidants of concern in this document. His conclusion was that "the ambient air measurements indicate that ozone may serve directionally, but cannot be expected to serve quantitatively, as a surrogate for the other products" (Altshuller, 1983). He found a greater correspondence between aldehydes and their organic precursors than between aldehydes and ozone. He found also that the correspondence between ozone and PAN concentrations (as well as PPN, H_2O_2, and HCOOH) is greater by far than the ozone-aldehyde relationship.

In summary, the significance for public health or welfare of the imposition of an additional oxidant burden from non-ozone oxidant rests on the answers to three basic questions:

1. Do PAN, PPN, H_2O_2, or HCOOH, singly or in combination, elicit adverse or potentially adverse responses?
2. Do any or all of these non-ozone oxidants act additively or synergistically in combination with ozone to elicit adverse or potentially adverse responses? Do any or all act antagonistically with ozone?
3. Do the time course and magnitude of the concentrations of these non-ozone oxidants parallel the time course and magnitude of ozone concentrations in the ambient air?

Given the information on health and welfare effects presented in subsequent chapters, coupled with the aerometric data presented in Chapter 6, the relationship between ozone and PAN concentrations is the specific relationship of most concern in this document.

1.6 EFFECTS OF OZONE AND PEROXYACETYL NITRATE ON VEGETATION

1.6.1 EFFECTS OF OZONE ON VEGETATION

1.6.1.1 Introduction. Foliar injury to vegetation is one of the earliest and most obvious manifestations of ozone injury to vegetation. The effects of ozone are not limited, however, to visible injury. Although plant foliage is the primary site of injury, secondary effects from ozone can occur. They include reduced plant growth of both roots and foliage, decreased yield, changes in crop quality, and alterations in susceptibility to biotic and abiotic stresses.

Ozone exerts a phytotoxic effect only if a sufficient amount reaches the sensitive cellular sites within the leaf. Ozone diffuses from the ambient air into the leaf through the stomata, which can exert some control on ozone uptake, to the active sites within the leaf. Ozone injury will not occur (1) if the rate of ozone uptake is low enough that the plant can detoxify or metabolize ozone or its metabolites; or (2) if the plant is able to repair or compensate for the effects of ozone (Tingey and Taylor, 1982). This is analogous to the response of plants to sulfur dioxide (SO_2) (Thomas et al., 1950). Cellular disturbances that are not repaired or compensated for are ultimately expressed as visible injury to the leaf or as secondary effects that can be expressed as reduced root growth, reduced yield of fruits or seeds, or both.

Plant growth and yield are the end products of a series of biochemical and physiological processes related to uptake, assimilation, biosynthesis, and translocation. Sunlight drives those processes that convert carbon dioxide into the organic compounds (photosynthesis) necessary for plant growth and development. The mineral nutrients and water necessary for plant growth are extracted by the plant from the soil. Plant organs then convert these raw materials into a wide array of compounds required for plant growth and yield. A disruption or reduction in the rates of uptake, assimilation, or subsequent biochemical reactions will be reflected in reduced plant growth and yield. Ozone would be expected to reduce plant growth or yield: (1) if it directly affected the plant process that was limiting plant growth; or (2) if it affected another step sufficiently such that this process became the step limiting plant growth (Tingey, 1977). Conversely, ozone will not limit plant growth if the process affected is not or does not become rate-limiting. This implies that not all the effects of ozone on plants are reflected in growth or yield reductions. This also suggests that there are combinations of ozone concentration and exposure duration that the plant can experience that will not result in visible injury or reduced plant growth and yield. Indeed, numerous studies have demonstrated combinations of concentration and time that did not cause a significant detectable effect on plant growth or yield.

Ozone induces a diverse range of effects on plants and plant communities. These effects are usually classified as either injury or damage. Injury encompasses all plant reactions such as reversible changes in plant metabolism (e.g., altered photosynthesis), leaf necrosis, altered plant quality, or reduced growth that do not impair yield or intended use of the plant (Guderian, 1977). In contrast, damage or yield loss includes all effects that reduce the intended use or the value of the plant, such as a reduction in the quantity or in aesthetic value; or any impairment in the intended use of the plant. For example, visible foliar injury to ornamental plants, detrimental responses in native species, and reductions in fruit and grain production are all considered as damage or yield loss. Although it is not always classified as damage, the occurrence of foliar injury is an indication that phytotoxic concentrations of ozone are present. In areas displaying foliar injury, additional studies should be conducted to assess the risk of ozone to vegetation and to determine if the intended use or value of the plants is being impaired.

1.6.1.2 Limiting Values of Plant Response. Several approaches have been used to estimate the ozone concentrations and exposure durations that induce foliar injury. Most of these studies have used short-term exposures (less than 1 day) and have measured visible injury as the response variable. In one approach to estimating the concentrations and durations that would induce specific amounts of visible injury, plants were exposed to a range of ozone concentrations and exposure durations and the resulting data were evaluated by regression analysis (Heck and Tingey, 1971). Data for several species were summarized to illustrate the range of concentrations required to induce foliar injury (5 and 20 percent) on sensitive, intermediate, and less sensitive species (Table 1-8).

An alternative approach for estimating the ozone concentrations and exposure durations that induce foliar injury is to use limiting-value analysis (Jacobson, 1977). The limiting-value method was developed from a review of the literature and represents the lowest concentration and exposure duration reported to cause visible injury on various plant species. The analysis was based on more than 100 studies of agricultural crops and 18 studies of tree species. The analysis yielded the following range of concentrations and exposure durations that are likely to induce foliar injury (U.S. Environmental Protection Agency, 1978).

TABLE 1-8. OZONE CONCENTRATIONS FOR SHORT-TERM EXPOSURES THAT PRODUCE 5 OR 20 PERCENT INJURY TO VEGETATION GROWN UNDER SENSITIVE CONDITIONS[a]

Exposure time, hr	Sensitive plants	Intermediate plants	Less sensitive plants
0.5	0.35 to 0.50 (0.45 to 0.60)	0.55 to 0.70 (0.65 to 0.85)	≧0.70 (0.85)
1.0	0.15 to 0.25 (0.20 to 0.35)	0.25 to 0.40 (0.35 to 0.55)	≧0.40 (0.55)
2.0	0.09 to 0.15 (0.12 to 0.25)	0.15 to 0.25 (0.25 to 0.35)	≧0.30 (0.40)
4.0	0.04 to 0.09 (0.10 to 0.15)	0.10 to 0.15 (0.15 to 0.30)	≧0.25 (0.35)
8.0	0.02 to 0.04	0.07 to 0.12	≧0.20 (0.30)

[a] The concentrations in parenthesis are for the 20% injury level. Table from U.S. Environmental Protection Agency (1978).

1. Agricultural crops:
   0.20 to 0.41 ppm for 0.5 hr
   0.10 to 0.25 ppm for 1.0 hr
   0.04 to 0.09 ppm for 4.0 hr

2. Trees and shrubs:
   0.20 to 0.51 ppm for 1.0 hr
   0.10 to 0.25 ppm for 2.0 hr
   0.06 to 0.17 ppm for 4.0 hr

It should be emphasized that both approaches estimate concentrations and exposure durations that might induce visible injury but that they cannot be used to predict impacts on crop yield or intended use. It should also be emphasized that both approaches are still considered valid.

The concept of limiting values has also been used to estimate the ozone concentrations and exposure durations which could potentially reduce plant growth and yield (U.S. Environmental Protection Agency, 1978). The data were analyzed and plotted in a manner similar to the appraoch of Jacobson (1977) (Figure 1-4). In Figure 1-4 the line bounds mean ozone concentrations and exposure durations below which effects on plant growth and yield were not detected.

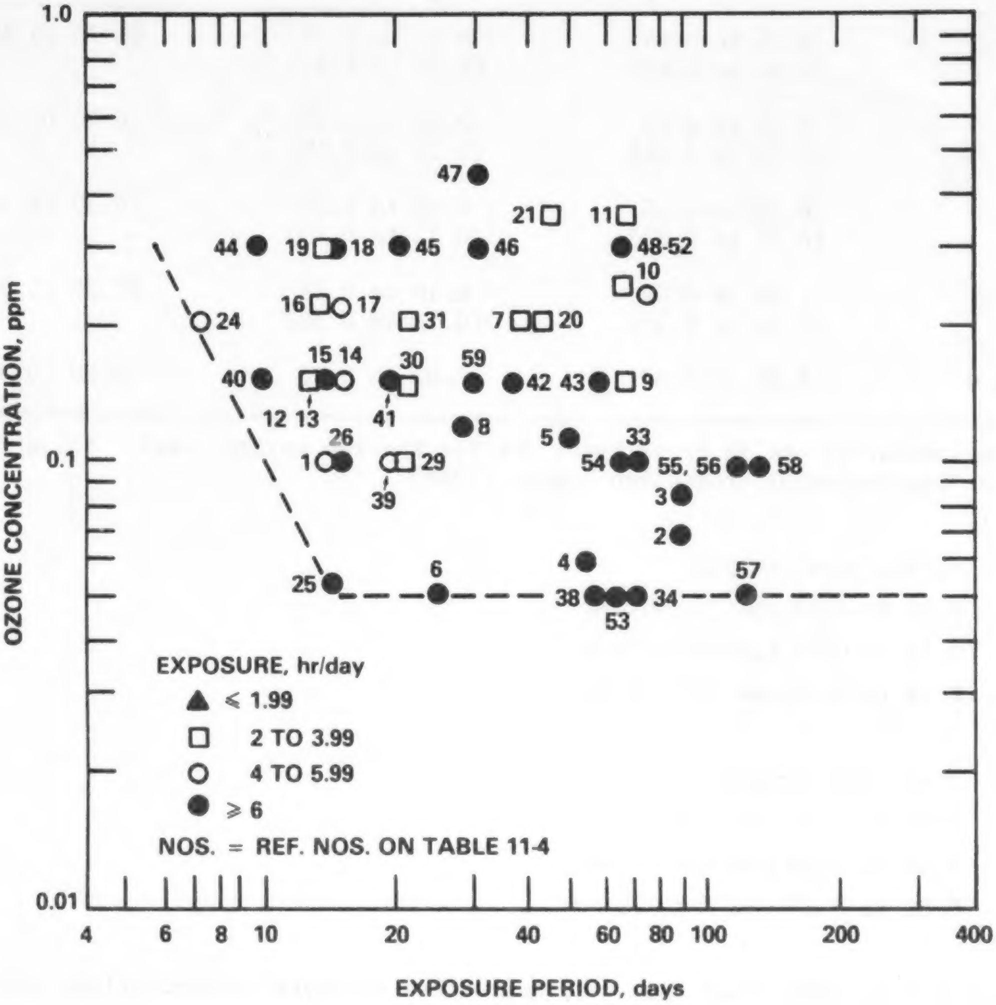

Figure 1-4. Relationship between O_3 concentration, exposure duration, and a reduction in plant growth or yield (see Table 7-18; also U.S. EPA, 1978).
Source: U.S. Environmental Protection Agency (1978).

This graphical analysis used data from both greenhouse and field studies and indicates that the lower limit for reduced plant performance is a mean ozone concentration of 0.05 ppm for several hours per day for exposure periods greater than 16 days. The O_3 response threshold increases to about 0.10 ppm at 10 days and to about 0.30 ppm at 6 days.

1.6.1.3 Methods for Determining Ozone Yield Losses. Diverse experimental procedures have been used to study the effects of ozone on plants, including studies under highly controlled conditions, exposures in open-top chambers, and field exposures without chambers. In general, the more controlled conditions are most appropriate for investigating specific responses and for providing the scientific basis for interpreting and extrapolating results. These systems are powerful tools by which to gain increased understanding of the biological effects of air pollutants. To assess the impact of ozone on plant yield, however, it is desirable to minimize deviations from the typical environment in which the plant is grown. For field crops, this implies that the studies should be conducted in the field, but for crops that are typically grown in glass houses, the studies should be conducted under glass-house conditions.

To improve estimates of yield loss in the field, the National Crop Loss Assessment Network (NCLAN) was initiated by EPA in 1980 to estimate the magnitude of crop losses caused by O_3 (Heck et al., 1982). The primary objectives of NCLAN were:

1. To define the relationships between yields of major agricultural crops and O_3 exposure as required to support the needs of economic assessments and the development of National Ambient Air Quality Standards;
2. To assess national economic consequences resulting from the exposure of major agricultural crops to O_3; and
3. To advance the understanding of the cause and effect relationships that determine crop responses to pollutant exposures.

The NCLAN experimental sites were selected on the basis of (1) differing climatic conditions, (2) distribution of crop species, and (3) the existence of established research groups studying air pollution effects on plants. Cultural conditions at these sites approximate typical agronomic practices and open-top field exposure chambers are used to minimize perturbations of the plant environment during the exposure. The investigators involved have attempted to use realistic O_3 concentrations and sufficient replication to permit the development of exposure-response models. The data have been analyzed using regression approaches. The exposures are characterized by a 7-hr (9:00 a.m. to 4:00 p.m.) seasonal mean O_3 concentration. This is the time period during which O_3 is added to the exposure chambers.

1.6.1.4 Estimates of Yield Loss. Studies, frequently using open-top exposure chambers, have been conducted to estimate the effects of O_3 on the yield of various crop species. These studies can be grouped into two types, depending on the experimental design and statistical methods used to analyze the data: (1) studies in which predictive equations relating O_3 exposure to plant response were developed; and (2) studies in which discrete treatment levels were compared to a control. The advantage of the regression approach is that exposure-response models can be used to interpolate results between treatment levels. Both types of experimental design, however, provide useful data for determining the effects of O_3 on plants.

In the NCLAN studies, ozone was added to either charcoal-filtered or ambient air to create the range of O_3 concentrations that is required when the regression approach is used to estimate O_3-induced yield loss. In summarizing the data, O_3-induced yield loss was derived from comparing performance of O_3-exposed plants to that of plants in charcoal-filtered air. Various regression techniques have been used to derive exposure-response functions. The use of regression approaches permits the estimation of the effects of O_3 on plant yield over the range of concentrations, not just at the treatment means, as is the case with analysis of variance methods. Examples of graphs of exposure-response equations and the data used to derive them show the fit of the various models to the experimental data (Figure 1-5).

Linear regression equations have been used to estimate yield loss but for some species and cultivars there appear to be systematic deviations from the data even though the equations had high coefficients of determination (r^2). The use of plateau-linear or polynomial equations appeared to fit the data better. More recently, a Weibull model has been used that yields a curvilinear response line providing a reasonable fit to the data. This model has also been used to develop yield response equations, combining the responses for several cultivars of a species (Figure 1-6). Statistical analysis indicates that for most crops the model fits the combined data, as well as the data for the individual cultivars. Yield losses for some major crop species were estimated using the combined models. It appears that O_3 affects the yield of corn and wheat much less than it does the yields of cotton, soybeans, and peanuts.

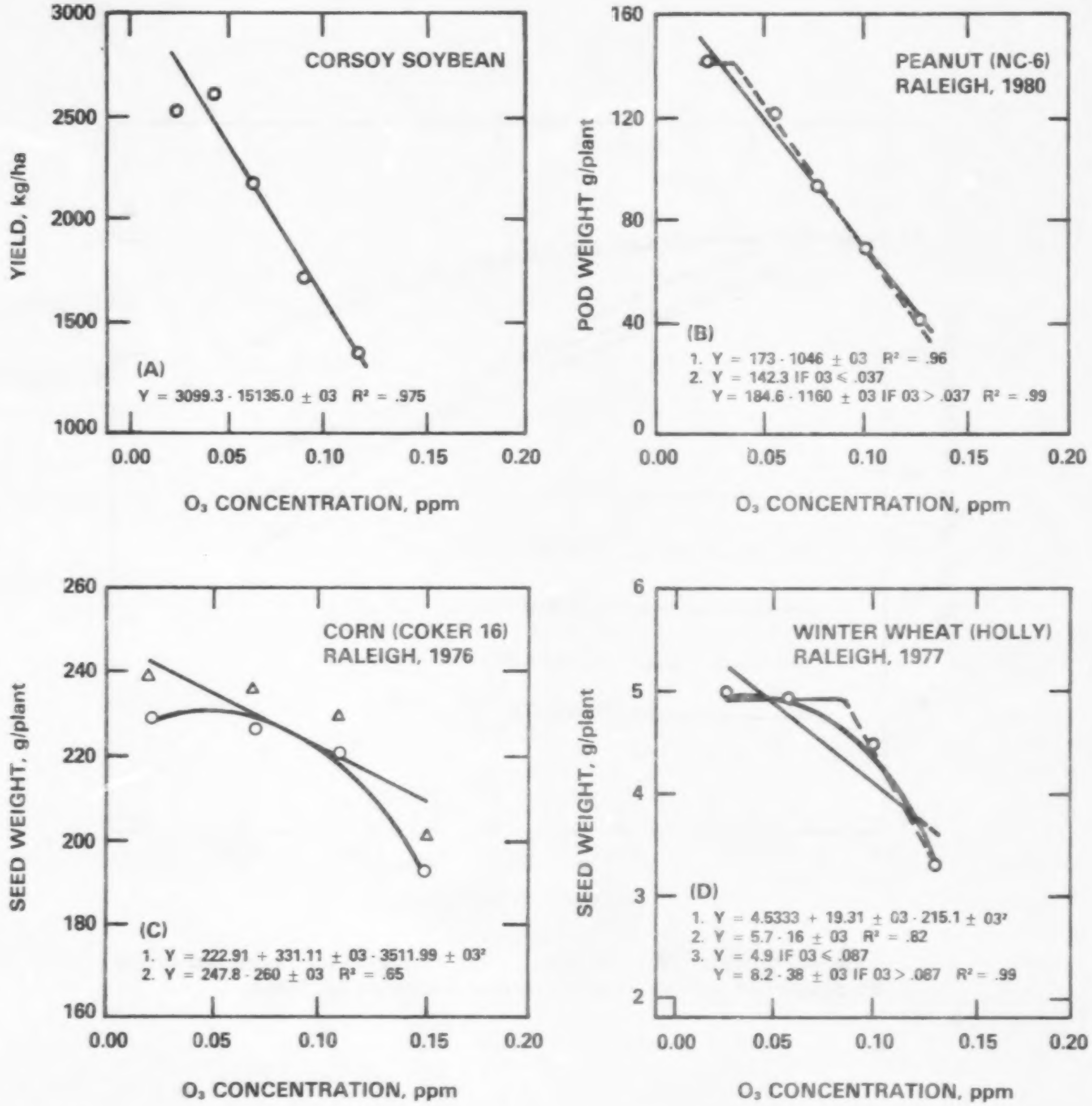

Figure 1-5. Examples of effects of O_3 exposure on yield of various plants. O_3 concentration (ppm) is expressed as 7-hr seasonal mean. Soybean (A) data from Kress and Miller (1983); peanut (B) data from Heagle et al., (1983) and Heck et al., (1982); corn (C) and wheat (D) data from Heagle and Heck (1980) and Heck et al., (1982).

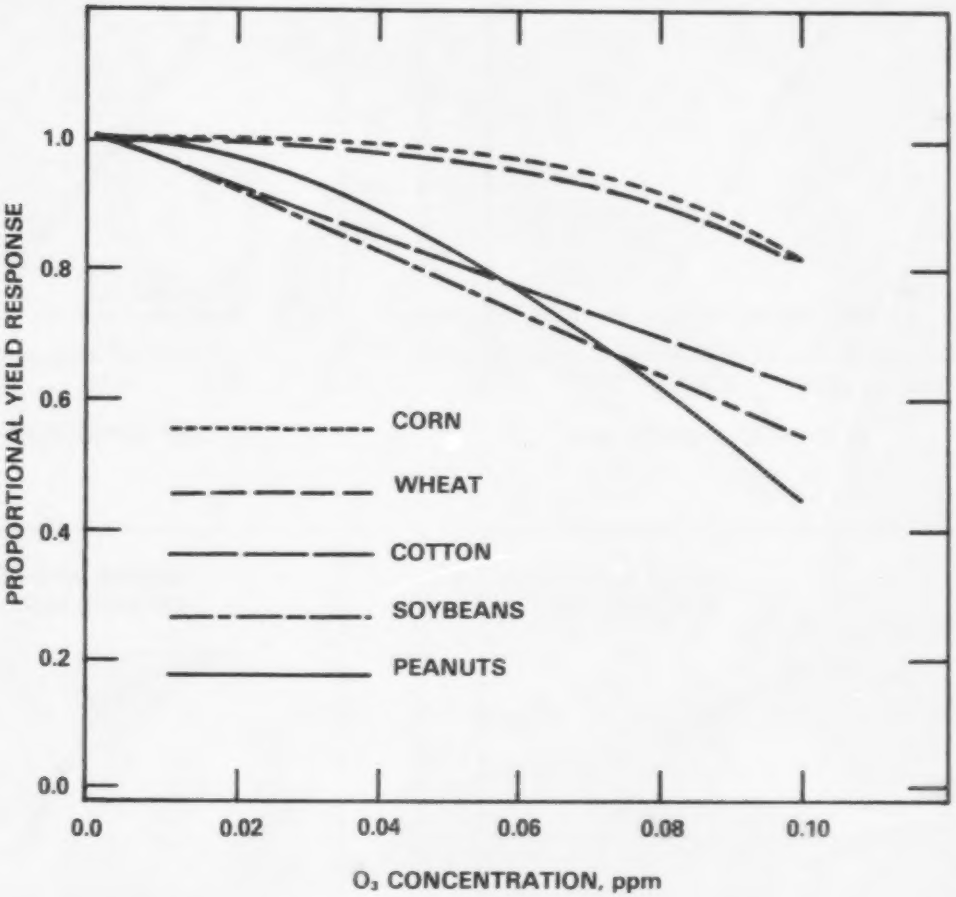

Figure 1-6. Relative O_3-induced yield reduction of selected crops as predicted by the Weibull model (Heck et al., 1983).

The yield response models can be used to estimate the O_3 concentrations that induce losses (e.g., 10 and 30 percent losses) in various plant species and cultivars (Table 1-9). In general, when several models were fit to the data they tended to predict similar concentrations that induced yield losses. In the case of corn, turnip, and winter wheat, however, the linear model tended to underestimate the O_3 concentrations that would cause 10 or 30 percent yield reductions. The similarity among the estimated concentrations for a given cultivar suggests that the predicted values are influenced to a greater extent by the original data than by the model used to describe the data. A brief review of the data (Table 1-9) indicates that for several species, mean yield reductions of 10 percent were predicted when the 7-hr seasonal mean O_3 concentration exceeded 0.04 to 0.05 ppm.

In addition to the studies in which regression approaches were used, various other approaches have been used to investigate the effects of O_3 treatments that were different from the control, rather than to develop exposure-response equations. In general, these data were analyzed using analysis of variance. Table 1-10 summarizes concentrations of O_3 reported to produce a loss of 10 percent in the yield of a number of crops. To summarize the data from studies that used discrete treatments, the lowest O_3 concentration that significantly reduced yield was determined from the analyses of the authors (Table 1-10). The lowest concentration reported to reduce yield was frequently the lowest concentration used in the study; hence, it was not always possible to estimate a no-effect exposure level. In general, the data indicate that O_3 concentrations of 0.10 ppm (frequently the lowest concentration used in the studies) for a few hours per day for several days to weeks generally caused significant yield reductions. Although it appears from this analysis that a higher O_3 concentration was required to cause an effect than estimated from the regression studies, it should be noted that the concentrations derived from the regression studies were based on a 10 percent yield loss, while in studies using analysis of variance (Table 1-10) the 0.10 ppm concentration frequently induced mean yield losses of 10 to 50 percent.

The data from the previous criteria document (U.S. Environmental Protection Agency, 1978) were used to develop limiting values that suggested that O_3 concentrations of 0.04 to 0.06 ppm for 4 hours or more were likely to injure plant foliage. The growth data summarized in that document indicated that plant growth and yield can be reduced at O_3 concentrations of 0.05 to 0.08 ppm for several

TABLE 1-9. SEASONAL 7-hour OZONE CONCENTRATIONS (ppm) AT WHICH YIELD LOSSES OF 10 PERCENT OR 30 PERCENT ARE PREDICTED FROM EXPOSURE-RESPONSE MODELS

Plants	Model	Control O_3 Concentration	Yield Loss 10%	Yield Loss 30%	Reference
Grains/Seeds					
Soybean					
(Corsoy)	Kg/ha = 3099.3 - 15135 x O_3	0.022	0.040	0.077	Kress and Miller, 1983
(Corsoy)	g/plant = 15.6 exp $[-(O_3/0.129)^{1.70}]$	0.022	0.043	0.076	Heck et al., 1983
(Davis)	seed wt/m = 534.5 - 3988.6xO_3+10960xO_3^2	0.025	0.038	0.070	Heagle et al., 1983
(Davis)	g/plant = 31.1 exp $[-(O_3.\ 0.129)^{0.91}]$	0.025	0.038	0.071	Heck et al., 1983
(Essex)	g/plant = 18.7 exp $[-(O_3/0.309)^{0.78}]$	0.014	0.037	0.109	Heck et al., 1983
(Hodgson-F)[*]	g/plant = 15.2 exp $[-(O_3/0.207)^{0.80}]$	0.017	0.039	0.096	Heck et al., 1983
(Hodgson-P)[*]	g/plant = 15.5 exp $[-(O_3/0.153)^{1.87}]$	0.017	0.043	0.084	Heck et al., 1983
(Williams)	g/plant = 19.4 exp $[-O_3/0.243)^{0.94}]$	0.014	0.038	0.098	Heck et al., 1983
Peanut - 1979[+]	pod wt/plant = 112 - 563 x O_3	0.026	0.043	0.078	Heagle et al., 1983
Peanut - 1980[*]	pod wt/plant = 173 - 1046 x O_3	0.025	0.039	0.067	Heagle et al., 1983
Peanut - 1980	pod wt/plant = 142.3 if $O_3 \leq 0.037$; if $O_3 > 0.037$ PW/P = 184.6 - 1160 x O_3	0.025	0.049	0.073	Heck et al., 1982
Peanut - 1980	g/plant - 148 exp $[-(O_3/0.186)^{3.20}]$	0.025	0.046	0.073	Heck et al., 1983
Kidney bean	seed wt/plant = 17.44 - 35.51 x O_3	0.025	0.072	0.165	Kohut and Lawrence, 1983
Kidney bean	g/plant = 16.5 exp $[-(O_3/0.287)^{1.77}]$	0.025	0.086	0.164	Heck et al., 1983
Field Corn					
(Coker 16)	g/plant 247.8 - 260 x O_3	0.02	0.113	0.300	Heck et al., 1982
(Coker 16)	g/plant = 222.91+331.11 x O_3- 3511.99 x O_3^2	0.02	0.132	-	Heagle & Heck, 1980
(Coker)	g/plant = 240 exp $[-(O_3/0.221)^{4.48}]$	0.02	0.133	0.175	Heck et al., 1983
(PAG 397)	g/plant = 166 exp $[-(O_3/0.160)^{4.28}]$	0.15	0.095	0.126	Heck et al., 1983
(Pioneer 3780)	g/plant = 149 exp $[-(O_3/0.155)^{3.11}]$	0.15	0.075	0.111	Heck et al., 1983
Winter wheat					
(Blueboy II)	g/plant = 6.6 - 18 x O_3	0.03	0.063	0.131	Heck et al., 1982
(Blueboy II)	g/plant = 5.908 + 3.958 x O_3 - 137.7 x O_3^2	0.03	0.0187	0.129	Healge and Heck, 1980
(Blueboy II)	g/plant = 5.88 exp $[-(O_3/0.175)^{3.22}]$	0.03	0.088	0.127	Heck et al., 1983
(Coker 47-27)[+]	g/plant = 5.8 - 21 x O_3	0.03	0.055	0.104	Heck et al., 1982
(Coker 47-27)	g/plant = 5.765 - 18.79 x O_3 - 20.00 x O_3^2	0.03	0.055	0.103	Heagle and Heck, 1980
(Coker 47-27)	g/plant 5.19 exp - $[-(O_3/0.171)^{2.06}]$	0.03	0.064	0.107	Heck et al., 1983
(Holly)[+]	g/plant = 5.7 - 16 x O_3	0.03	0.063	0.128	Heck et al., 1982
(Holly)	g/plant = 4.533 + 19.31 x O_3- 215.1 x O_3^2	0.03	0.095	0.129	Heck et al., 1982
(Holly)	g/plant = 4.95 exp $[-(O_3/0.156^{4.95}]$	0.03	0.099	0.127	Heck et al., 1983
(Holly)	g/plant = 4.9 if x $\leq$ 0.087 if $O_3 > 0.087$ g/p = 8.2 -38 O_3	0.03	0.100	0.126	Heck et al., 1982

TABLE 1-9. SEASONAL 7-hour OZONE CONCENTRATIONS (ppm) AT WHICH YIELD LOSSES OF 10 PERCENT OR 30 PERCENT PREDICTED FROM EXPOSURE-RESPONSE MODELS (continued)

Plants	Model	Control O_3 Concentration	Yield Loss		Reference
			10%	30%	
(Oasis)[+]	g/plant = $4.9 - 12 \times O_3$	0.03	0.068	0.143	Heck et al., 1982
(Oasis)	g/plant = $4.475 + 3.320 \times O_3 - 93.49 \times O_3^2$	0.03	0.088	0.138	Heagle and Heck, 1980
(Oasis)	g/plant = $4.88 \exp [-(O_3/0.186)^{3.20}]$	0.03	0.093	0.135	Heck et al., 1983
Cotton	g/plant = $41.5 \exp [-(O_3/0.197)^{1.12}]$	0.018	0.041	0.092	Heck et al., 1983
Root Crops					
Turnip					
(Just Right)[+]	edible rt wt/plant = $12.9 - 94 \times O_3$	0.014	0.026	0.051	Heck et al., 1982
(Just Right)	edible rt wt/plant = 10.7 if $O_3 \leq 0.038$ if $O_3 > 0.038 = 15.5 - 127 \times O_3$	0.014	0.046	0.063	Heck et al., 1982
(Just Right)	g/plant = $10.89 \exp [-(O_3/0.090)^{3.05}]$	0.014	0.043	0.064	Heck et al., 1983
(Purple Top White Globe)	edible rt wt/plant = $7.2 - 49 \times O_3$	0.014	0.027	0.054	Heck et al., 1982
(Purple Top White Globe)	edible rt wt/plant = 6.0 if $O_3 \leq 0.034$ if > 0.034 ERW/P = $8.1 - 60 \times O_3$	0.014	0.045	0.065	Heck et al., 1982
(Purple Top White Globe)	g/plant = $6.22 \exp [-(O_3/0.095)^{2.51}]$	0.014	0.040	0.064	Heck et al., 1983
(Shogoin)[+]	edible rt wt/plant = $5.3 - 36 \times O_3$	0.014	0.027	0.054	Heck et al., 1982
(Shogoin)	g/plant = $4.68 \exp (-(O_3/0.096)^{2.12}]$	0.014	0.036	0.060	Heck et al., 1983
(Tokyo Cross)[+]	edible rt wt/plant = $18.1 - 116 \times O_3$	0.014	0.028	0.057	Heck et al., 1982
(Tokyo Cross)	edible rt wt/plant = 14.8 if $O_3 \leq 0.054$ if $O_3 > 0.054$ ERW/P = $27.0 - 226 \times O_3$	0.014	0.061	0.074	Heck et al., 1982
(Tokyo Cross)	g/plant = $15.25 \exp [-(O_3/-.094)^{3.94}]$	0.014	0.053	0.072	Heck et al., 1983
Foliage Crops					
Lettuce	fresh hd wt/plant = $1065.7 - 5978 \times O_3$	0.043	0.057	0.084	Heck et al., 1982
Lettuce	g/plant = $1245 \exp [-(O_3/0.098)^{1.22}]$	0.043	0.053	0.075	Heck et al., 1983
Spinach (America)	g/plant = $22.7 - 106\ O_3$ if $O_3 > 0.087$ g/p = $8.2 - 38\ O_3$	0.024	0.043	0.081	Heck et al., 1982
(Winter Bloomsdale)	g/plant = $23.3 - 121 \times O_3$	0.024	0.041	0.075	Heck et al., 1982
(Winter Bloomsdale)	g/plant = $20.8 \exp [-(O_3/0.127)^{2.07}]$	0.024	0.049	0.080	Heck et al., 1983
(Hybrid 7)	g/plant = $42.1 - 193 \times O_3$	0.024	0.043	0.082	Heck et al., 1982
(Hybrid 7)	g/plant = $36.6 \exp [-(O_3/0.139)^{2.68}]$	0.024	0.060	0.095	Heck et al., 1983
(Viroflay)	g/plant = $46.1 - 238 \times O_3$	0.024	0.041	0.075	Heck et al., 1982
(Viroflay)	g/plant = $41.1 \exp [-(O_3/0.129)^{1.99}]$	0.024	0.048	0.080	Heck et al., 1983

*The Hodgson data were obtained from two designs in 1981; a full harvest (F) and a partial plot harvest (P), where some plants were removed prior to harvest.

*This model did not fit the data well and tended to underestimate the O_3 concentrations which cause yield losses.

TABLE 1-10. OZONE CONCENTRATIONS AT WHICH SIGNIFICANT YIELD LOSSES HAVE BEEN NOTED FOR A VARIETY OF PLANT SPECIES EXPOSED TO O_3 UNDER VARIOUS EXPERIMENTAL CONDITIONS

Plant species	Exposure duration	Yield reduction, % of control	O_3 concentration, ppm	Reference
Alfalfa	7 hr/d, 70 d	51, top dry wt	0.10	Neely et al., 1977
Alfalfa	2 hr/d, 21 d	16, top dry wt	0.10	Hoffman et al., 1975
Pasture grass	4 hr/d, 5d/wk, 5 wk	20, top dry wt	0.09	Horsman et al., 1980
Ladino clover	6 hr/d, 5 d	20, shoot dry wt	0.10	Blum et al., 1982
Soybean	6 hr/d, 133 d	55, seed wt/plant	0.10	Heagle et al., 1974
Sweet corn	6 hr/d, 64 d	45, seed wt/plant	0.10	Heagle et al., 1972
Sweet corn	3 hr/d, 3 d/wk, 8 wk	13, ear fresh wt	0.20	Oshima, 1973
Wheat	4 hr/d, 7 d	30, seed yield	0.20	Shannon and Mulchi, 1974
Radish	3 hr	33, root dry wt	0.25	Adedipe and Ormrod, 1974
Beet	2 hr/d, 38 d	40, storage root dry wt	0.20	Ogata and Maas, 1973
Potato	3 hr/d, every 2 wk, 120 d	25, tuber wt	0.20	Pell et al., 1980
Pepper	3 hr/d, 3 d/wk, 11 wk	19, fruit dry wt	0.12	Bennett et al., 1979
Cotton	3 hr/d, 2 d/wk, 13 wk	62, fiber dry wt	0.25	Oshima et al., 1979
Carnation	24 hr/d, 12 d	74, no of flower buds	0.05-0.09	Feder and Campbell, 1968
Coleus	2 hr	20, flower no.	0.20	Adedipe et al., 1972
Begonia	4 hr/d, once every 6 d for a total of 4 times	55, flower wt	0.25	Reinert and Nelson, 1979
Ponderosa pine	6 hr/d, 126 d	21, stem dry wt	0.10	Wilhour and Neely, 1977

TABLE 1-10. OZONE CONCENTRATIONS AT WHICH SIGNIFICANT YIELD LOSSES HAVE BEEN NOTED FOR A VARIETY OF PLANT SPECIES EXPOSED TO O_3 UNDER VARIOUS EXPERIMENTAL CONDITIONS (continued)

Plant species	Exposure duration	Yield reduction, % of control	O_3 concentration, ppm	Reference
Western white pine	6 hr/d, 126 d	9, stem dry wt	0.10	Wilhour and Neely, 1977
Loblolly pine	6 hr/d, 28 d	16, height growth	0.05	Wilhour and Neely, 1977
Pitch pine	6 hr/d, 28 d	13, height growth	0.10	Wilhour and Neely, 1977
Poplar	12 hr/d, 5 mo	+1333, leaf abscission	0.041	Wilhour and Neely, 1977
Hybrid poplar	12 hr/d, 102 d	58, height growth	0.15	Patton, 1981
Hybrid poplar	8 hr/d, 5 d/wk, 6 wk	50, shoot dry wt	0.15	Patton, 1981
Red maple	8 hr/d, 6 wk	37, height growth	0.25	Dochinger and Townsend, 1979
American sycamore	6 hr/d, 28 d	9, height growth	0.05	Kress and Skelly, 1982
Sweetgum	6 hr/d, 28 d	29, height growth	0.10	Kress and Skelly, 1982
White ash	6 hr/d, 28 d	17, total dry weight	0.15	Kress and Skelly, 1982
Green ash	6 hr/d, 28 d	24, height growth	0.10	Kress and Skelly, 1982
Willow oak	6 hr/d, 28 d	19, height growth	0.15	Kress and Skelly, 1982
Sugar maple	6 hr/d, 28 d	12, height growth	0.15	Kress and Skelly, 1982

hours per day. These concentrations are similar to the concentrations (0.04 to 0.07 ppm) shown in this document to reduce plant yield in field studies (using various approaches) and in ambient air studies.

1.6.1.5 Effects on Crop Quality. Although only a few studies have been reported, O_3 can also reduce crop quality in addition to reducing the total yield of the crop. Quality is a general term that includes many features of the crop such as nutritional composition, appearance, taste, and ability to withstand storage and shipment. Examples of O_3-induced alterations in quality are decreased oil in soybean seeds (Howell and Rose, 1980; Kress and Miller, 1983); decreased β-carotene, vitamin C, and carbohydrates in alfalfa (Thompson et al., 1976; Neely et al., 1977); and increased reducing sugars in potatoes, which are associated with undesirable darkening when potatoes are used to make potato chips (Pell et al., 1980).

1.6.1.6 Yield Loss from Ambient Exposures. Of the studies done to determine the impact of ambient air oxidants (primarily O_3) on plant yield, most have compared the yield differences between plants grown in ambient air and those grown in charcoal-filtered air. Early research documented that ambient oxidants reduced the yield and quality of citrus, grape, tobacco, cotton, and potato (U.S. Environmental Protection Agency, 1978). More recent studies have substantiated the effects of ambient oxidants on plant yield. Ozone has been shown to induce significant yield reductions in tomato and bean (MacLean and Schneider, 1976), soybean (Howell et al., 1979), two sweet corn cultivars (Thompson et al., 1976), and in native plants (forbes, grasses, and sedges) (Duchelle et al., 1983). In a study conducted over several years, bean yields varied from a 5 percent increase to a 22 percent decrease in response to O_3 concentrations in excess of 0.06 ppm (Heggestad et al., 1980). Studies conducted on eastern white pine in the southern Appalachian mountains have shown that exposure to O_3 in ambient air has reduced the radial growth of sensitive individual trees 30 to 50 percent annually over the last 15 to 20 years (Mann et al., 1980; Benoit et al., 1982). Field studies in the San Bernardino National Forest have shown that during the last 30 years exposure to ambient air O_3 reduced height growth of ponderosa pine by 25 percent, radial growth by 37 percent, and the total wood volume produced by 84 percent (Miller and Elderman, 1977).

1.6.1.7 Statistics Used to Characterize Ozone Exposures. The characterization and representation of plant exposures to O_3 has been, and continues to be, a major problem. Research has not yet clearly identified which components of the pollutant exposure cause the plant response. Most studies have characterized the exposure by the use of mean O_3 concentrations, although various averaging times have been used. Some studies have also used cumulative O_3 dose. The difficulty of selecting an appropriate statistic by which to characterize plant exposure has been summarized by Heagle and Heck (1980). Ambient and experimental O_3 exposures have been presented in published studies as seasonal, monthly, weekly, or daily means; peak hourly means; number of hours above a selected concentration; or the number of hours above selected concentration intervals. None of these statistics have adequately characterized the relationship among O_3 concentration, exposure duration, interval between exposures, and plant response. The use of a mean concentration implies that all concentrations of O_3 are equally effective in causing plant responses and minimizes the contributions of the peak concentrations to the response. The mean treats low-level long-term exposures the same as high-concentration short-term exposures. Most of the reported exposure statistics are not directly correlated with each other and it is difficult to relate them to ambient air measurements of O_3, which are usually reported as 1-hr means. Also it is difficult to transform one exposure statistic to another without reanalyzing the original air monitoring data.

Studies with beans and tobacco (Heck et al., 1966) showed that a dose (concentration x time) over a short period induced more injury than the same dose distributed over a longer period. Tobacco studies showed that the O_3 concentration was approximately twice as important as exposure duration in causing foliar injury (Tonneijck, 1984). In beans, foliar injury was shown to occurred when the internal O_3 flux exceeded 5500 $\mu g\ m^{-2}$ in 1 hr (Bennett, 1979). A single 3-hr exposure, however, at approximately half the concentration (0.27 compared with 0.49 ppm) required a 64 percent greater internal flux of O_3 to produce the same amount of foliar injury as the 1-hr exposure. The greater importance of concentration compared to exposure duration has been reported by numerous authors (e.g., Heck and Tingey, 1971; Henderson and Reinert, 1979; Reinert and Nelson, 1979).

Not only are concentration and time important, but also the dynamic nature of the O_3 exposure; i.e., is the exposure at a constant or variable concentration? Musselman et al. (1983) recently showed that constant concentrations of O_3 caused the same kinds of effects in plants as variable concentrations at equivalent doses; but, the variable concentration exposures caused a greater effect than the constant exposures. Studies with radishes exposed to ambient air ozone showed that significant yield reductions occurred when the daily maximum O_3 concentration exceeded 0.06 ppm at least 10 percent of the days or more (Ashmore, 1984). In soybeans, reduced yield (weight/seed) was most closely correlated with the number of O_3 peaks in excess of 0.10 ppm (Pratt, 1982). Studies with SO_2 have also shown that plants exposed to variable concentrations exhibited a greater plant response than those exposed to a constant concentration (McLaughlin et al., 1979; Male et al., 1983).

1.6.1.8 Relation Between Yield Loss and Foliar Injury. Because plant growth and production depends on photosynthetically functional leaves, various studies have been conducted to determine the association between foliar injury and yield for species in which the foliage is not part of the yield. Some research has demonstrated significant yield loss with little or no foliar injury (e.g., Tingey et al., 1971; Tingey and Reinert, 1975; Kress and Skelly, 1982; Feder and Campbell, 1968; Adedipe et al., 1972). Other studies showed that significant foliar injury did not always cause a yield loss (Heagle et al., 1974; Oshima et al., 1975). The relative sensitivities of two potato cultivars were reversed when judged by foliar injury versus yield reductions (Pell et al., 1980). In field corn, foliar injury occurred at a lower O_3 concentration than yield reductions; but as the O_3 concentration increased, yield was reduced to a greater extent than foliar injury was increased (Heagle et al., 1979a). In wheat, foliar injury was not a good predictor of O_3-induced yield reductions (Heagle et al., 1979b).

1.6.1.9 Physiological Basis of Yield Reductions. As discussed earlier in this summary, plant growth is the summation of a series of biochemical and physiological processes related to uptake, assimilation, biosynthesis, and translocation. Am impairment in these processes may lead to reduced plant yeild if the process is limiting.

For growth to occur, plants must assimilate carbon dioxide and convert it into organic substances; thus, an inhibition in carbon assimilation (photosynthesis) may be reflected in altered plant growth or yield. In several species O_3 (at 0.05 ppm and higher) inhibited photosynthesis, as measured by gas-exchange (e.g., U.S. Environmental Protection Agency, 1978; Coyne and Bingham, 1978; Black et al., 1982). Biochemical studies showed that O_3 (0.12 ppm for 2 hr) inhibited an enzyme that catalyzes the assimilation of carbon dioxide (Pell and Pearson, 1983).

In addition to decreasing the total amount of carbon dioxide that is assimilated, ozone alters the pattern by which the reduced amount of assimilate is partitioned throughout the plant. There is generally less photosynthate translocated to the roots and to the reproductive organs (e.g., Tingey et al., 1971; Jacobson, 1982; Oshima et al., 1978, 1979; Bennett et al., 1979). This reduces root size and vigor as well as marketable yield.

Reproductive capacity (flowering and seed set) is reduced by O_3 in ornamental plants, soybean, corn, wheat, and some other plants (Adedipe et al., 1972a, Feder and Campbell, 1968; Heagle et al., 1972, 1974; Shannon and Mulchi, 1974). These data suggest that O_3 impairs the fertilization process in plants. This suggestion has been confirmed in tobacco and corn studies using low concentrations (0.05 to 0.06 ppm) of O_3 (Feder, 1968; Mumford, 1972).

Ozone both in field and chamber studies stimulates premature senescence and leaf drop (Menser and Street, 1962; Heagle et al., 1974; Heggestad, 1973; Pell et al., 1980; Hofstra et al., 1978). In part, the O_3-induced yield reductions have been attributed to premature senescence. The premature leaf drop and senescence decrease the amount of photosynthate that a leaf can contribute to plant growth and yield and also the time during which the leaf contributes.

1.6.1.10 Factors Affecting Plant Response to Ozone. Numerous factors influence the type and magnitude of plant response to O_3. Most studies of the factors influencing plant response have been limited to effects on foliar injury, although some studies have measured yield and a few have examined the physiological basis for such influences. The factors studied include environmental factors, biological factors, and interactions with other air pollutants.

1.6.1.10.1 Environmental conditions. Environmental conditions before and during plant exposure are more influential in determining the magnitude of the plant response than post-exposure conditions. The influence of environmental factors has been studied primarily under controlled conditions but field observations have substantiated the results. Most studies have evaluated the influence of only a single environmental factor and, in most, foliar injury was the plant response measured. Some generalizations of the influence of environmental factors can be made.

1. Light conditions that are conducive to stomatal opening appear to enhance O_3 injury (U.S. Environmental Protection Agency, 1978). Light is required to induce stomatal opening permitting the plant to absorb pollutants.

2. No consistent pattern relating plant response to temperature has been observed (U.S. Environmental Protection Agency, 1978), although plants do not appear to be sensitive at extremely high or low temperatures.

3. Plant injury tends to increase with increasing relative humidity (U.S. Environmental Protection Agency, 1978). The relative humidity affect appears to be related to stomatal aperture, which tends to increase with increasing relative humidity. McLaughlin and Taylor (1980) demonstrated that plants absorb significantly more O_3 at high humidity than at low humidity. It is generally accepted that plants in the eastern United States are injured by lower concentrations of O_3 than their counterparts in California . This difference has been attributed to differences in humidity (U.S. Environmental Protection Agency, 1978).

4. As soil moisture decreases, plant water stress increases and there is a reduction in plant sensitivity to O_3 (U.S. Environmental Protection Agency, 1978). The reduced O_3 sensitivity is apparently related to stomatal closure, which reduces O_3 uptake (U.S. Environmental Protection Agency; Olszyk and Tibbits, 1981; Tingey et al., 1982). Water stress does not confer a permanent tolerance to O_3; once the water stress is alleviated the plants regain their sensitivity to O_3 (Tingey et al., 1982).

1.6.1.10.2 Interaction with plant diseases. Ozone affects the development of disease in plant populations. Most laboratory evidence suggests that O_3 (at ambient concentrations or greater for 4 or more hours) inhibits infection by pathogens and subsequent disease development (Laurence, 1981; Heagle 1982; U.S. Environmental Protection Agency, 1978). Increases, however, in diseases from "stress pathogens" have been noted. For example, plants exposed to O_3 were more readily injured by *Botrytis* spp. than plants not exposed to O_3 (Manning et al., 1970a,b; Wukasch and Hofstra 1977a,b; Biseassar, 1982). Both field and laboratory studies have confirmed that the roots and cut stumps of O_3-injured ponderosa and Jeffrey pines are more readily colonized by a root rot (*Heterobasidion annosum*). The degree of infection was correlated with the foliar injury (James et al., 1980a; Miller et al., 1982). Studies in the San Bernardino National Forest showed that O_3-injured trees were predisposed to attack by bark beetles and that fewer bark beetles were required to kill an O_3-injured tree (Miller et al., 1982).

1.6.1.10.3 Interaction of ozone with other air pollutants. The report of Menser and Heggestad (1966) provided the initial impetus for studying the interaction of O_3 with SO_2. They showed that Bel W-3 tobacco plants exposed to O_3 (0.03 ppm) or SO_2 (0.24 to 0.28 ppm) were uninjured but that substantial foliar injury resulted when the plants were exposed to both gases simultaneously. Subsequent studies (both greenhouse and field) have confirmed and extended the observation that combinations of O_3 and SO_2 frequently cause more visible injury than expected based on the injury from the individual gases. This injury enhancement (synergism) is most common at low concentrations of each gas and also when the amount of foliar injury induced by each gas, individually, is small. At higher concentrations, or when extensive injury occurs, the effects of the individual gases tends to be less than additive (antagonistic). The effects of pollutant combinations has also been investigated in relation to other plant effects besides foliar injury, and these have been discussed in several reviews and numerous individual reports (e.g., Reinert et al., 1975; Ormrod, 1982; Jacobson and Colavito, 1976; Heagle and Johnston, 1979; Olszyk and Tibbitts, 1981).

There have been fewer studies of the effects of O_3 and SO_2 on plant yield than on visible injury (Flagler and Younger, 1982a; Foster et al., 1983; Heggestad and Bennett, 1981; Heagle et al., 1983a). In field studies, the addition of SO_2 to O_3 generally did not influence the O_3 response unless the concentrations and exposure frequencies were greater than those of SO_2 that typically occur in the ambient air of the United States.

The applicability of the yield results from pollutant combination studies to ambient conditions is not known. An analysis of ambient air monitoring data indicated that at sites where the two pollutants were co-monitored, 10 or fewer periods of co-occurrence occurred during the growing season (Lefohn and Tingey, 1984). Co-occurrence was defined as the simultaneous occurrence of hourly-average concentrations of 0.05 ppm or greater for both pollutants. At this time, it appears that most of the studies of the effects on pollutant cominations (O_3 and SO_2) on plant yield have used a higher frequency of exposure duration and pollutant co-occurrence than occurs in the ambient air.

Only a few studies have investigated the effects of O_3 with other pollutants and no clear trend is available. Preliminary studies using three-pollutant mixtures (O_3, SO_2, NO_2) showed that the addition of SO_2 and NO_2 (at low concentrations) caused a greater growth reduction than O_3 alone.

1.6.1.11 Economic Assessment of Ozone Effects Ozone has been identified as the most important air pollutant in terms of spatial distribution and impacts on agricultural yields. Given the importance of United States agricultural products to both domestic and world consumption of food and fiber, significant reduction in their supply would have substantial economic consequences.

Various methods have been used to assess the economic impact of O_3, many of which have been simplistic. Reliable assessment procedures should use theoretically justified economic methodologies that consider the effects to both the producer and consumer. These methods usually address price changes resulting from adjustments in production and the role of producer input and output substitution strategies. The resulting estimates more accurately assess the true economic impact than other procedures.

Numerous studies have attempted to assess the dollar losses to crop production that result from exposures to ozone in ambient air. The quality of these various estimates is variable. For example, the economic loss data cited in the previous criteria document (U.S. Environmental Protection Agency, 1978) used simplistic traditional approaches that were not well-based theoretically. Therefore, the previous estimates should be viewed with caution. Most of the economic assessments of agricultural losses since the last criteria document (U.S. Environmental Protection Agency, 1978) have focused on regional losses. Crop loss estimates for southern California ranged from 45 million (Adams et al., 1982) to approximately 100 million dollars (Leung et al., 1982). These studies used different assessment methodologies and considered the effects of ozone on different crops. The economic impact of ozone on corn, wheat, and soybeans for the "Corn Belt" was estimated at 688 million dollars (Adams and McCarl, 1984), while for Illinois alone the losses were estimated at 55 to 200 million dollars (Mjelde et al., 1984).

Only a few studies have attempted to assess the national economic consequences of ambient ozone. Nationwide economic losses have been estimated to be between approximately 2 billion (SRI, 1981; Adams and Crocker, 1982b) and 3 billion dollars (Shriner et al., 1982). These estimates include more complete dose-response information for an increasing number of major commodities and better air quality data than previous national estimates (U.S. Environmental Protection Agency, 1978). These estimates should be considered preliminary, however, since two of the three studies used simple traditional approaches.

In summary, the current dollar estimates of crop damage are useful primarily as indicators of the magnitudes of impact. A full accounting of the economic mechanisms underlying agricultural production is required to provide definitive estimates of the extent of agricultural losses. Such accounting should include both annual and perennial crops (agronomic and horticultural) and the associated dynamic adjustments of agricultural production. It must consider the effects on intermediate consumers, such as livestock growers and food processors, and final consumers, both domestic and foreign. The effect of O_3 on ornamentals, both physically and economically, has also never been addressed.

1.6.2 Effects of Peroxyacetyl Nitrate on Vegetation

1.6.2.1 Introduction. Peroxyacetyl nitrate (PAN) is an extremely phytotoxic air pollutant that is produced by photochemical reactions similar to those that produce ozone. The sequence of events within the plant leading to the effects of PAN is conceptually similar to that described for O_3, except that the pollutants apparently have different reactive sites within the cells. The symptoms of photochemical oxidant injury that were originally described (prior to 1960) have subsequently been shown to be identical with the symptoms produced by PAN. Following the identification of PAN as a phytotoxic air pollutant, PAN injury (foliar symptoms) has been observed throughout California and in several other states and foreign countries.

1.6.2.2 Factors Affecting Plant Response to PAN. Herbaceous plants are sensitive to PAN and cultivar differences in sensitivity have been observed in field and controlled studies. Trees and other woody species, however, are apparently resistant to visible foliar injury (Taylor, 1969; Davis, 1975, 1977).

There is an absolute requirement for light before, during, and after exposure or visible PAN injury will not develop (Taylor et al., 1961). Field observations have shown that crops growing under moisture stress developed little or no injury during photochemical oxidant episodes while, adjacent to them, recently irrigated crops were severely injured (Taylor, 1974).

Only a few studies have investigated the effects of PAN and O_3 mixtures on plants. When plants were exposed to both gases at their respective injury thresholds, no interaction between the gases was found (Tonneijck, 1984). At higher concentrations, the effects were less than additive. Studies with petunia confirmed that O_3 tended to reduce PAN injury (Nouchi et al., 1984).

1.6.2.3 Limiting Values of Plant Response. The limiting-value method has been used to estimate the lowest PAN concentration and exposure duration reported to cause visible injury on various plant species (Jacobson, 1977). The analysis yielded the following range of concentrations and exposure durations likely to induce foliar injury: (1) 200 ppb for 0.5 hr; (2) 100 ppb for 1.0 hr; and (3) 35 ppb for 4.0 hr.

More recent studies, however, suggest that these values need to be lowered by 30 to 40 percent to reduce the likelihood of foliar injury (Tonneijck, 1984). For example, foliar injury developed on petunia plants exposed at 5 ppb PAN for 7 hours (Fukuda and Terakado, 1974). Under field conditions, injury symptoms may develop on sensitive species when PAN concentrations reach approximately 15 ppb for 4 hours (Taylor, 1969).

1.6.2.4 Effects of PAN on Plant Yield. Only limited studies have been conducted to determine the effects of PAN on plant growth and yield. In greenhouse studies, radish, oat, tomato, pinto bean, beet, and barley were exposed to PAN concentrations of up to 40 ppb for 4 hours per day, twice per week, from germination to crop maturity (Taylor et al., 1983). No significant effects on yield were detected. This is supportive of field observations, in which foliar injury occurred on these species from ambient PAN exposures but no evidence was seen of reduced yield in these crops. In contrast, lettuce and Swiss chard exposed to PAN concentrations of up to 40 ppb for 4 hours per day, twice a week, from germination to crop maturity showed yield losses up to 13 percent (lettuce) and 23 percent (Swiss chard) without visible foliar injury symptoms (Taylor et al., 1983). The results indicate that PAN at concentrations below the injury threshold can cause significant yield losses in sensitive cultivars of leafy vegetable crops. In addition to reduced yield without visible injury, photochemical oxidant events have caused foliar injury on leafy vegetables (Middleton et al., 1950). After severe PAN damage, entire crops may be unmarketable or else extensive hand work may be required to remove the injured leaves before the crop may be marketed.

A comparison of PAN concentrations likely to cause either visible injury or reduced yield with the measured ambient concentrations (Chapter 6) indicates that it is unlikely that PAN effects will occur to plants in the United States except in some areas of California and in possibly a few other localized areas.

1.7 EFFECTS OF OZONE AND OTHER PHOTOCHEMICAL OXIDANTS ON NATURAL ECOSYSTEMS

1.7.1 Introduction

Temperate forest ecosystems within the United States currently are experiencing declines. Tree responses, unless they are the result of a specific biotic disease or an acute pollutant exposure, are cumulative and frequently the culmination of a number of chronic stresses (Figure 1-7). Among chronic stresses to which trees are exposed is air pollution.

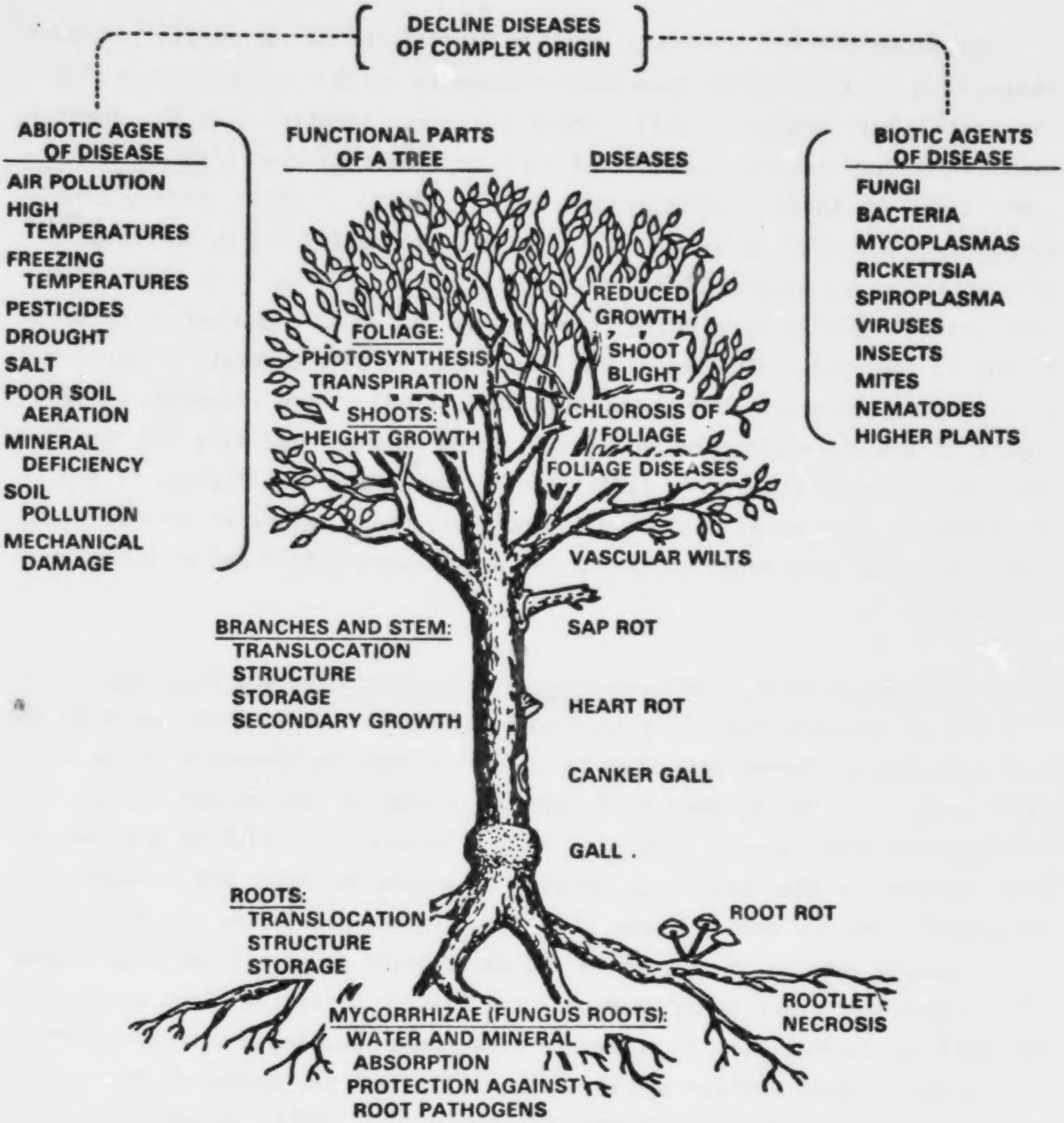

Figure 1-7. Summation of abiotic and biotic agents involved in diseases of trees, given by types of diseases and functional parts of the tree. Decline diseases are caused by a combination of biotic and abiotic agents.

Source: Manion (1981).

The mixed-conifer forests of the San Gabriel and San Bernardino mountain ranges east of Los Angeles have been exposed to oxidant air pollution since the early 1950s (Miller, 1973). Ozone was first identified as the agent responsible for the slow decline and death of ponderosa pine (Pinus ponderosa Laws) trees in these forests (Miller et al., 1963). Later, Jeffrey pine (Pinus jeffreyi Grev. & Balf.) was also found to be injured by O_3 exposure. Oxidant injury of eastern white pine (Pinus strobus L.) has been observed for many years in the eastern United States. It was first reported as needle blight in the early 1900s but in 1963 was shown to be the result of acute and chronic ozone exposure (Berry and Ripperton, 1963). More recently, oxidant injury of eastern white pine in the Blue Ridge Mountains of Virginia has been reported by Hayes and Skelly (1977) and on the Cumberland Plateau of east Tennessee by Mann et al. (1980). In addition, ozone injury in natural plant communities has been reported by Treshow and Stewart (1973) and by Duchelle et al. (1983).

1.7.2 Oxidant-induced Effects on a Western Coniferous Forest Ecosystem

One of the most thoroughly studied ecosystems in the United States is the mixed coniferous forest ecosystem in the San Bernardino Mountains of southern California. The San Bernardino Forest is located at the eastern end of the 80-mile-long South Coast Air Basin, where a severe air pollution problem has been created by the last three decades of extensive urban and industrial development (Miller and Elderman, 1977). Oxidants carried by the marine air flow probably entered the forest in the early 1940s or soon after when vegetation injury was first recognized near the coast. Sensitive plant species in the National Forest, such as ponderosa pine, began showing unmistakable injury in the early 1950s (Miller and Elderman, 1977), but the source of the injury was not identified as O_3 until 1962 (Miller et al., 1963). Extensive visible injury and concern about the possible adverse effects of chronic O_3 exposure on an important forest ecosystem led to an interdisciplinary study. From 1973 to 1978, a study was conducted to determine the response of the organisms and biological processes of the conifer forest to chronic oxidant exposures and to interpret responses within the ecosystem context (Miller et al., 1982).

The ecosystem processes analyzed were: (1) carbon flow (the movement of carbon dioxide into the plant; its incorporation into green plant organic matter; and then its partitioning among consumers, litter, decomposers, and the soil; and its return to the atmosphere); (2) the movement of water in the soil-plant-atmosphere continuum; (3) mineral nutrient flow through the green plant litter and soil-water compartments; and (4) the shift in diversity patterns in time and space as represented by changes in composition of tree species in stands, age, structure, and density.

All of the ecosystem processes mentioned above were shown by the study to be affected directly or indirectly. Foliar injury of sensitive ponderosa and Jeffrey pine was observed when O_3 concentrations ranged from 0.05 to 0.06 ppm. During the period of study, average 24-hr O_3 concentrations during the months May through September ranged from a background of 0.03 to 0.04 ppm to a maximum of 0.10 to 0.12 ppm.

Less sensitive trees, in decreasing order of sensitivity, were white fir (_Abies_ _concolor_ Lindl.), black oak (_Quercus_ _kelloggii_ Newb.), incense cedar (_Libocedrus_ _decurrens_ Torr.), and sugar pine (_Pinus_ _lambertiana_ Dougl.). Associated with foliar injury were a decrease in photosynthesis, a reduction in tree growth (both height and diameter), and a reduction in seed production in ponderosa and Jeffrey pine. Foliar injury, premature needle fall, and senescence decreased the amount of foliage capable of conducting photosynthesis and a reduction in carbohydrates decreased the capacity of the remaining foliage. Carbon flow in the form of carbohydrates diminished as stressed trees retained smaller amounts of assimilated carbon after transpiration losses. The amounts of mineral nutrients in the living foliage of injured ponderosa pines were lower than in needles on healthy trees. The store of carbon and mineral nutrients accumulated in the thick needle layers under stands of O_3-injured trees and their movement back into the trees was curtailed. Nutrient availability was influenced by a reduction in the number of species and the population density of the fungi that normally colonize living needles and later participate in decomposition, because the usual increase that occurs with age was prevented by premature needle senescence and abscission (Miller et al., 1982). Stressed trees showed a decrease in the number of mycorrhzial rootlets and their replacement by small saprophytic fungi in the small rootlets of stressed trees (Parmeter et al., 1962) Mycorrhizae are very sensitive to the photosynthetic capacity of the host and to the capacity of the host to translocate carbon compounds to the roots (Hacskaylo, 1973).

A comparison of the radial growth of ponderosa pine during years (1910 to 1940) of low pollution (<0.03 ppm) with years (1941 to 1971) of high pollution (0.03 to 0.12 ppm) indicate that O_3 exposure reduced the average annual radial growth by approximately 40 percent, height by 25 percent, and wood volume by

84 percent in trees less than 30 years of age. The marketable volume of trees 30 years of age was reduced by 83 percent in the areas with the highest O_3 concentrations.

Stressed pines also became more susceptible to root rot (Heterobasidion annosum) and pine beetle (Dendroctonus brevicomis), as the result of weakening of the host by photochemical oxidants. Photochemical oxidant injury of ponderosa pines results in reduced oleoresin yield, rate of flow and exudation pressure, moisture of phloem and sapwood, and phloem thickness. All of these are believed to be important in the defense of the tree against bark beetles (Stark and Cobb, 1969). Studies also indicate that a disease-insect relationship exists between root-infecting fungi and bark beetles. Approximately 80 percent of the ponderosa pines infested with bark beetles had been infected by root-disease fungi prior to beetle infestation (Stark and Cobb, 1969). Verticicladiella wagenerii was the major fungus attacking the roots. The fungus moves from tree to tree via the roots. Heterobasidion annosum was likewise found to have infected conifer roots prior to beetle attack. Heterobasidion usually does not become a serious problem in California forests, however, until disturbances by humans, such as logging, have occurred (Stark and Cobb, 1969). Mortality rate of the trees reached 2 to 3 percent in some years. Injured ponderosa and Jeffrey pines older than 130 years produced significantly fewer cones per tree than uninjured trees of the same age (Luck, 1980). Heavy litter accumulation occurred in stands with the most severe needle injury and defoliation. Pine seed establishment was hindered by litter depth, but the growth of oxidant-tolerant understory species was encouraged. Buildup of litter and the presence of easily ignited foliage on smaller trees could lead to destructive fires. Removal by O_3 and by fires of the pine-dominated forest and the reduction of competition among remaining trees leads to a dominance in these forests of self-perpetuating, fire-adapted, O_3-tolerant shrub and oak species mixtures that provide fewer commodity and amenity values than the former pine forest and that inhibit reestablishment of pines and other conifers.

Any mature natural community transfers 10 to 20 percent of the energy fixed by plants to herbivores (Woodwell, 1974). Consumer organisms constitute an extremely diverse group, and only a limited amount of information on their response to pollutants is available (Newman, 1979). The influence of oxidants on these organisms is assumed to be mainly through the food webs. At this time, studies have not indicated a direct impact of O_3 on the organisms themselves. The breakdown, however, of the processes of energy flow and nutrient cycling resulting from the disruption of photosynthesis, reproduction, or a structural change among the producers within ecosystems can affect consumers by removing their shelter and food source.

1.7.3 Effects of Ozone on Other Ecosystems

The responses that have been observed in the San Bernardino Forest ecosystem from O_3-associated stress have also been observed in other ecosystems within the United States that have been exposed to the same or lower ranges of O_3 concentrations.

Studies made along the Blue Ridge Parkway and on the Cumberland Plateau of east Tennessee support the view that exposure to O_3 reduces growth in sensitive trees (Benoit et al., 1982). Eastern white pine of reproducing age located in experimental plots situated along the Blue Ridge Parkway from the Shenandoah National Park in the north to the southernmost end of the Parkway in Virginia were studied to determine the radial increment during the 1955 to 1978 period. Growth of trees classified as sensitive was 25 percent less; and in trees classified as intermediate in sensitivity, growth was 15 percent less than in tolerant trees. Mean radial increments for all trees during the last 10 years of the study were smaller than for the previous 24 years. Comparison of growth during 1974 to 1978 with radial growth during 1955 to 1959 indicated a decrease in growth of 26, 37, and 51 percent for tolerant, intermediate, and sensitive trees. During the period of the study, concentrations of 0.05 to 0.07 ppm of O_3 were recorded on a recurring basis, with episodic peaks of 0.12 ppm or higher occurring (Benoit et al., 1982). Steady decline in annual ring increments of sensitive white pine was also observed on the Cumberland Plateau during the years 1962 to 1979 (McLaughlin et al., 1982). A reduction of 70 percent in average annual growth and 90 percent in average bole growth was observed in sensitive white pine when compared to both tolerant trees and trees of intermediate sensitivity. Annual occurrences of O_3 at hourly concentrations of 0.08 ppm or greater were associated with the growth reductions. Reduction in growth of sensitive white pine on the Blue Ridge Parkway and on the Cumberland Plateau, as in the case of the San Bernardino Mountains, was correlated with the predisposing symptoms of chronic decline, which includes the following sequence of events and conditions: (1) premature senescence and loss of older needles at the end of the growing season; (2) reduced storage capacity of carbohydrates in the fall and resupply capacity in the spring to support new needle growth; (3) increased reliance of new needles on self-support during growth;

(4) shorter new needles, resulting in lower gross photosynthetic productivity; (5) higher retention of current photosynthate by foliage resulting in reduced availability of photosynthate for external usage (including repair of chronically stressed tissues of older needles); and (6) premature casting of older needles (McLaughlin et al., 1982). Degeneration of feeder roots and mycorrhizae usually precedes the onset of above-ground symptoms (Manion, 1981). Decreases in nutrient and water uptake may also occur. These changes produce weakened trees. Weakened trees are, in turn, predisposed to attack by root-rot fungi such as Heterobasidion annosum, Verticicladella wagenerii, and V. procera, to defoliation by insects, and to attack by the pine beetle, Dendroctonus brevicomis.

Injury by O_3 to native herbaceous vegetation growing in the Virginia mountains was also observed (Duchelle et al., 1983). Ambient O_3 concentrations were shown to reduce growth and productivity of graminoid and forb vegetation in the Shenandoah National Park. For each year of the study, biomass production was greatest for vegetation grown in filtered-air chambers. The total 3-year cumulative dry weight for the filtered chambers was significantly ($P < 0.05$) different from non-filtered and open-air plots. Common milkweed (Ascelepias syrica L.) and common blackberry (Rubus allegheniensis Porter) were the only two native species to develop visible injury. Milkweed has been previously shown to be quite sensitive to O_3 (Duchelle and Skelly, 1981). Ozone episodes occurred several times each year during the period of the study. Peak hourly concentrations ranged from 0.08 to 0.12 ppm; however, monthly hourly average concentrations ranged from 0.03 to 0.06 ppm. The effects of O_3 in altering the natural vegetation of the Virginia mountains was not assessed. Lower biomass production could result in selection for vegetation better able to cope with the O_3 stress. As in California, O_3 is transported from distant sources to the Virginia mountains. In the Blue Ridge and Appalachian Mountains, these sources include the industrial midwest, eastern Virginia, and the Washington, D.C., area.

In Utah, Treshow and Stewart (1973) conducted one of the few studies concerned with the impact of air pollution on natural plant communities. Grassland, oak, aspen, and conifer communities in the Salt Lake Valley and Wasatch Mountains were studied. Some dominant species considered keys to community integrity were found to be sensitive. Bromus tectorum L. (cheatgrass), the most prevalent species in the grassland community, was also the most sensitive to O_3. Other grasses and forbs were not as sensitive (Table 1-11); however, in those grasses with visible injury, carbohydrate production was

TABLE 1-11. INJURY THRESHOLDS FOR 2-HOUR EXPOSURES TO OZONE

Species	Injury threshold, ppm O_3 for 2 hr	Species	Injury threshold, ppm O_3 for 2 hr
Grassland-oak community species:		Perennial forbs:	
Trees and shrubs:		Allium acuminatum Hook	0.25
Acer grandidentatum Nutt.	over 0.40	Angelica pinnata S. Wats.	under 0.25
Acer negundo L.	over 0.25	Aster engelmanni (Eat.) A. Gray	0.15
Arteresia tridentata Nutt.	0.40	Carex siccata Dewey	0.30
Mahonia repens G. Don	over 0.40	Cichorium intybus L.	0.25
Potentilla fruticosa L.	0.30	Cirsium arvense (L.) Scop.	under 0.40
Quercus gambelii Nutt.	0.25	Epilobium angustifolium L.	0.30
Toxicodendron radicans (L.) Kuntze	over 0.30	Epilobium watsoni Barbey	0.30
		Eriogonum heracloides Nutt.	0.30
Perennial forbs:		Fragaria ovalis (Lehm.) Rydb.	0.30
Achillea millefolium L.	over 0.30	Gentiana amarella L.	over 0.15
Ambrosia psilostachya DC.	over 0.40	Geranium fremontii Torr.	under 0.40
Calochortus nuttallii Torr.	over 0.40	Geranium richardsonii Fisch. & Traut.	0.15
Cirsium arvense (L.) Scop.	0.40	Juncus sp.	over 0.25
Conium maculatum L.	over 0.25	Lathyrus lanzwertii Kell.	over 0.25
Hedysarum boreale Nutt.	0.15	Lathyrus pauciflorus Fern.	0.25
Helianthus anuus L.	over 0.30	Mertensia arizonica Greene	0.30
Medocago sativa L.	0.25	Mimulus guttatus DC.	over 0.25
Rumex crispus L.	0.25	Mimulus moschatus Dougl.	under 0.40
Urtica gracilis Ait.	0.30	Mitella stenopetala Piper	over 0.30
Vicia americana Muhl.	over 0.40	Osmorhiza occidentalis Torr.	0.25
		Phacelia heterophylla Pursh	under 0.25
Grasses:		Polemonium foliosissimum A. Gray	0.30
Bromus brizaeformis Fish. & Mey.	0.30	Rudbeckia occidentalis Nutt.	0.30
Bromus tectorum L.	0.15	Saxifraga arguta D. Don	under 0.30
Poa pratensis L.	0.25	Senecio serra Hook.	0.15
Aspen and conifer community species:		Taraxacum officinale Wiggers	over 0.25
		Thalictrum fendleri Engelm.	over 0.25
Trees and shrubs:		Veronica anagallis-aquatica L.	0.25
Abies concolor (Gord. & Glend.) Lindl.	0.25	Vicia americana Muhl.	over 0.25
Amelanchier alnifolia Nutt.	0.20	Viola adunca Sm.	over 0.30
Pachystima myrsinites (Pursh) Raf.	over 0.30		
Populus tremuloides Michx.	0.15	Annual forbs:	
		Chenopodium fremontii Wats.	under 0.25
Ribes hudsonianum Richards.	0.30	Callomia linearis Nutt.	under 0.25
Rosa woodsii Lindl.	over 0.30		
Sambucus melanocarpa A. Gray	over 0.25	Descurainia californica (Gray) O.E. Schulz	0.25
Symphoricarpos vaccinioiders Rydb.	0.30	Galium bifolium Wats.	over 0.30
Perennial forbs:		Gayophytum racemosum T. & G.	0.30
Actaeu arguta Nutt.	0.25	Polygonum douglasii Greene	over 0.25
Agastache urticifolia (Benth.) Kuntze	0.20	Grasses:	
		Agropyron caninum (L.) Beauv.	over 0.25
		Bromus carinatus Hook. & Arn.	under 0.25

Source: Treshow and Stewart (1973).

significantly reduced. Aspen (Populus tremuloides Michx) was the most sensitive member of the aspen community. In both cases single 2-hr exposures to 0.15 ppm of O_3 caused severe injury. Removal of the dominant species (cheatgrass) from plant communities could result in a shift to another species. Decline in or removal of aspen could affect the growth of white fir because seedlings require the shade provided by aspen for optimal juvenile growth. Loss of aspen populations could influence forest succession by restricting white fir development, causing a shift from a forest to a grassland or forb vegetation community (Treshow and Stewart, 1973). In a companion study conducted in chambers in the greenhouse, O_3 exposures of 0.15 to 0.3 ppm for 2 hr per day reduced root and top growth, and fewer seeds were produced (Harwood and Treshow, 1975).

It is apparent that in natural communities exposed to O_3, the tolerant species would soon become the dominants. The authors concluded that O_3 must be considered a significant environmental parameter that influences the composition, diversity, and stability of natural plant communities.

The foregoing studies indicate that the impact of O_3 changes the composition and succession patterns of plant communities. The more mature stages of ecosystems use nutrients and energy more efficiently. Mature systems are tight; disturbances cause leakage. The leakage may be large enough under certain circumstances to in time reduce the potential of the site to support life (Woodwell, 1974). Changes that cause reductions in biotic structure are destabilizing and retrogressive. The entire array of plants is changed by disturbance from one in which large-bodied, long-lived species occur to one in which small-bodied, short-lived, rapidly reproducing plants predominate (Woodwell, 1974). This pattern is exemplified by the San Bernardino National Forest, where the mixed conifer forest is being replaced by low-growing shrubs and annual herbs. It is also occurring in the eastern United States, where the degradation of the Appalachian forests from North Carolina to Maine is currently taking place as the red spruce (Picea rubens Sarg.) and other large, long-lived species are being removed by at-present unknown forces (Johnson and Siccama, 1983). Also associated with the loss of stable ecosystems is the maintenance of normal water and climatic conditions, protection from wind and erosion, and protection from noise pollution (Guderian, 1977).

1.7.4 Interrelated Ecosystems

1.7.4.1 Aquatic Ecosystems. It is extremely important to consider that an adverse impact on a forest or agricultural ecosystem may in turn adversely affect adjacent aquatic systems. A variety of linkages for energy and nutrient exchange exist. Disruptions induced by air pollution stress on terrestrial ecosystems often trigger dysfunctions in neighboring aquatic ecosystems, such as streams, lakes, and reservoirs. Sediments resulting from erosion can change the physical character of stream channels, causing changes in bottom deposits, erosion of channel banks, obstruction of flow, and increased flooding. They can fill in natural ponds and reservoirs. Finer sediments can reduce water quality, affecting public and industrial water supplies and recreational areas. Turbidity caused by increased erosion can also reduce the penetration of light into natural waters. This, in turn, can reduce plant photosynthesis and lower supplies of dissolved oxygen, leading to changes in the natural flora and fauna (Bormann and Smith, 1980). Significant forest alterations, therefore, may have a regional impact on nutrient cycling, soil stabilization, sedimentation, and eutrophication of adjacent or nearby aquatic systems. Interfacing areas, such as wetlands and bogs, may be especially vulnerable to impact.

1.7.4.2 Agricultural Ecosystems. Natural and agricultural ecosystems possess the same basic functional components, require energy flow and mineral cycling for maintenance, and are subject to the dominating influences of climate and substrate. Natural ecosystems vary in diversity from simple systems with few species to complex systems with many species. Their populations also vary in genetic composition, age, and species diversity. They are self-regulating and self-perpetuating. Agroecosystems, on the other hand, are highly manipulated monocultures of similar genetic and age composition and are unable to maintain themselves without the addition of nutrients, energy, and human effort; opportunistic native and imported species may invade the sites. The manipulation of monocultures is designed to concentrate ecosystem productivity into a particular species to maximize its yield (e.g., corn, wheat, soybeans) for the benefit of humans (Cox and Atkins, 1979). If any of the species, varieties, or cultivars is very sensitive to O_3, its market value is destroyed. When this occurs, efforts are made to find a resistant cultivar, as with tobacco, or to grow a crop less sensitive to O_3 stress. Cost alone would prevent replacement of the variety of species in a natural ecosystem.

1.7.5 Ecosystem Responses to Stress

Ecosystems, because of their complexity, respond to stress in a manner different from individuals (Figure 1-8). Ecosystems respond to stress through the response of the organisms that compose them. Three main levels of interaction are involved: between the individual and its environment, the population

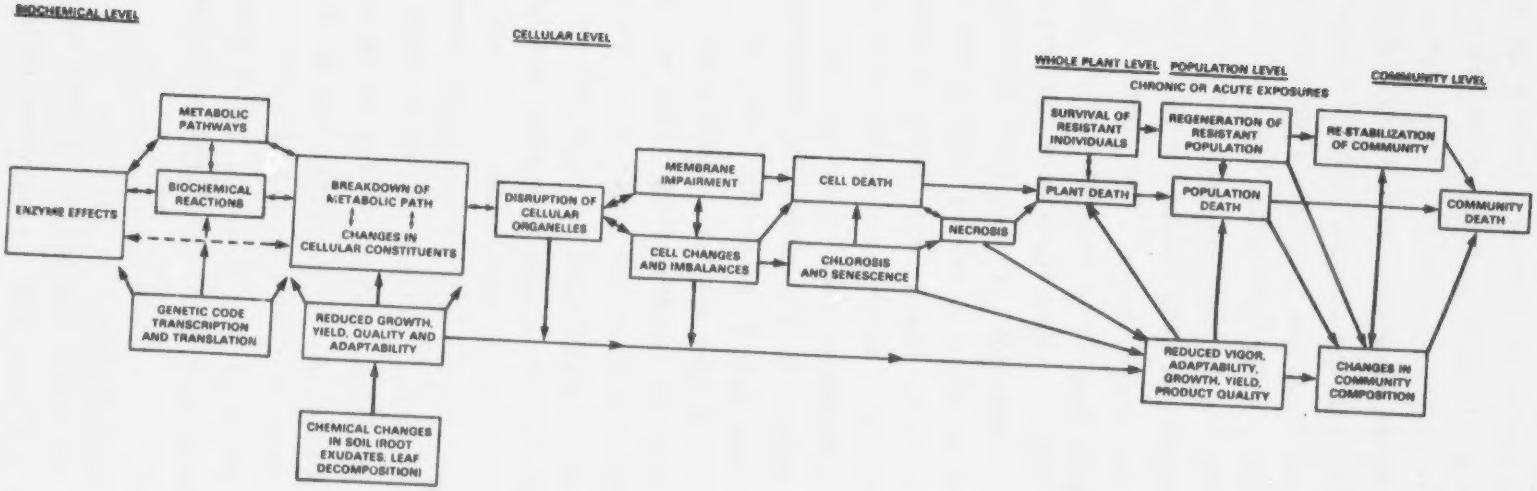
BIOCHEMICAL LEVEL
CELLULAR LEVEL
WHOLE PLANT LEVEL
POPULATION LEVEL
CHRONIC OR ACUTE EXPOSURES
COMMUNITY LEVEL
ENZYME EFFECTS
METABOLIC PATHWAYS
BIOCHEMICAL REACTIONS
GENETIC CODE TRANSCRIPTION AND TRANSLATION
BREAKDOWN OF METABOLIC PATH
CHANGES IN CELLULAR CONSTITUENTS
REDUCED GROWTH, YIELD, QUALITY AND ADAPTABILITY
CHEMICAL CHANGES IN SOIL (ROOT EXUDATES, LEAF DECOMPOSITION)
DISRUPTION OF CELLULAR ORGANELLES
MEMBRANE IMPAIRMENT
CELL CHANGES AND IMBALANCES
CELL DEATH
CHLOROSIS AND SENESCENCE
NECROSIS
SURVIVAL OF RESISTANT INDIVIDUALS
PLANT DEATH
REGENERATION OF RESISTANT POPULATION
POPULATION DEATH
RE-STABILIZATION OF COMMUNITY
COMMUNITY DEATH
REDUCED VIGOR, ADAPTABILITY, GROWTH, YIELD, PRODUCT QUALITY
CHANGES IN COMMUNITY COMPOSITION

Figure 1-8. Conceptual sequence of levels showing continuum of plant responses.
Source: Adapted from Heck (1973).

and its environment, and the ecosystem (the community and its environment) (Billings, 1978). Individual organisms of a population sensitive to environmental changes die or are unable to compete with resistant organisms, so that they do not reproduce. The capacity of an ecosystem to maintain internal stability is determined by the ability of individual organisms to adjust to change. The tolerance limit for an individual organism is determined by its genetic makeup and varies from organism to organism. The range of tolerance also varies depending on age, stage of growth, or growth form of an organism. Those organisms that are tolerant of or adapt best to stress contribute most to future generations, because they produce the greatest number of progeny in a population (Woodwell, 1970; Odum, 1971a; Smith, R. L., 1980; Roose et al., 1982). Some plant populations have the capacity to evolve resistance (tolerance) to environmental stresses such as air pollution. Resistant plants are able to maintain normal growth and remain free from injury in a given polluted environment, but resistance is usually not complete (Roose et al., 1982). Variability in tolerance or resistance to air pollutants is common in most plant species.

The complexity of interrelationships within and between individuals in an ecosystem is summarized in Figure 1-8 (Heck, 1973). As this figure demonstrates, perturbations at any level of organization within an individual organism (biochemical, cellular, and whole plant levels) can affect one or more aspects of an ecosystem (population and community levels).

The ecosystem processes of energy flow and nutrient cycling are directly involved in plant growth and reporduction. The process of photosynthesis uses energy from the sun to convert carbon dioxide and water into carbohydrates. Nutrients enter plants through the roots and with the carbohydrates are converted into the wide array of compunds required for plant growth and reproduction. Alterations in these biochemical and physiological processes are the fundamental cause of all other plant effects (Figure 1-8).

1.8 EFFECTS OF OZONE AND OTHER PHOTOCHEMICAL OXIDANTS ON NONBIOLOGICAL MATERIALS

1.8.1 Introduction

Research conducted over a period of more than two decades has shown that ozone has the ability to react with both manmade and natural materials. While some research has been done on the effects of total oxidants, the only components of total oxidants studied individually are ozone and nitrogen dioxide.

Apparently no research has been done on the potential effects on materials of the peroxyacyl nitrates or of hydrogen peroxide. In spite of the research focus on ozone, however, the amount of damage from ozone to actual in-house materials remains poorly characterized.

The materials known to be most susceptible to ozone attack are elastomers, textile fibers and dyes, and certain types of paints. Ideally, the nature and amount of ozone damage to the materials can be approximated by physical damage functions in combination with ambient air concentrations. The economic impact from ozone-related damage can then be estimated by using accelerated replacement and repair costs or increased avoidance costs. None of these areas is sufficiently defined in the literature, however, to assess the amount and cost of oxidant-related damage.

1.8.2 Effects and Damage Functions

1.8.2.1 Elastomers. Virtually all the available literature on photochemical oxidant research focuses on ozone and its effects on economically abundant or important materials. The effects of ozone on elastomers are the best documented. Natural rubber and synthetic polymers such as polymers of styrene, butadiene, and isoprene, make up most of the elastomer production in the United States. These chemicals are used for formulating automotive tires and for protective electrical coverings. The mechanism of ozone degradation on elastomers shares similarities and differences with simple oxidation from atmospheric oxygen. Ozone damage is mainly a surface phenomenon, whereas damage from simple oxidation occurs internally. Ozone cracks occur at right angles to the direction of stress (Mueller and Stickney, 1970). Over time, the elastomer becomes hard and brittle, losing its physical integrity. In the absence of ozone and other photochemical oxidants, oxidation from atmospheric oxygen still occurs, but at a much slower rate and apparently by different mechanisms.

High humidity and mechanical stress greatly affect the formation, depth of cracking, and, in automotive tires, the adhesion between plies (Davies, 1979; Wenghoefer, 1974). Ozone affects natural rubber and other elastomers in a dose-related fashion.

Dose is defined in materials research as the product of concentration and duration of exposure. The importance of ozone dose was demonstrated by Bradley and Haagen-Smit (1951), who used a specially formulated ozone-sensitive natural rubber (NR). Samples exposed to ozone at a concentration of 20,000 ppm cracked almost instantaneously, and those exposed to lower concentrations took a proportionately longer time to crack. At concentrations of 0.02 to 0.46 ppm, and under 100-percent strain, the cracking rate was proportional to the time of exposure, from 3 to 65 min. Cracking occurred at a rate of 0.02 to 0.03 ppm-hr over the entire range of concentrations.

Similar findings were reported by Edwards and Storey (1959), who exposed two styrene-butadiene rubber (SBR) elastomers to ozone at a concentration of 0.25 ppm for 19 to 51 hr under 100-percent strain. With ozone doses of 4.75 ppm-hr to 12.75 ppm-hr, a proportional rate in cracking depth was observed, averaging 2.34 µm/hr for cold SBR and 4.01 µm/hr for hot SBR. When antiozonants were added to the compounds, the reduction in cracking depth rate was proportional to the amount added. Haynie et al. (1976) exposed samples of a tire sidewall to ozone at concentrations of 0.08 and 0.5 ppm for 250 to 1000 hr under 10 and 20 percent-strain. Under 20-percent strain, the mean cracking rate for 0.08 ppm was 1.94 µm/hr. From these and other data, they estimated that at the ozone standard of the time (0.08 ppm, 1-hr average), and at the annual NO_x standard of 0.05 ppm, it would take 2.5 years for a crack to penetrate cord depth.

In addition to stress, factors affecting the cracking rate include atmospheric pressure, humidity, sunlight, and other atmospheric pollutants. Veith and Evans (1980) found a 16-percent difference in cracking rates reported from laboratories located at various geographic elevations.

Ozone has been found to affect the adhesion of plies (rubber-layered strips) in tire manufacturing. Exposure to ozone concentrations of 0.05 to 0.15 ppm for a few hours significantly decreased adhesion in an NR/SBR blend, causing a 30-percent decrease at the highest ozone level. This adhesion problem worsened at higher relative humidities. When fast-blooming waxes and antiozonants or other antioxidants were added, only a combination of protective measures allowed good adhesion and afforded protection from attack by ozone and sunlight. Wenghoefer (1974) showed that ozone (up to 0.15 ppm), especially in combination with high relative humidity (up to 90 percent), caused greater adhesion losses than heat and NO_2 did, with or without high relative humidity.

1.8.2.2 Textile Fibers and Dyes. The effects of ozone on dyes have been known for nearly three decades. In 1955, Salvin and Walker exposed certain red and blue anthraquinone dyes to 0.1 ppm ozone and noted fading, which until that time had been thought to be caused by NO_2. Subsequent work by Schmitt

(1960, 1962) confirmed the fading action of ozone and the importance of relative humidity in the absorption and reaction of ozone in vulnerable dyes. The acceleration in fading of certain dyes by high relative humidity was noted later by Beloin (1972, 1973) at an ozone concentration of 0.05 ppm and a relative humidity of 90 percent. Kamath et al. (1982) also found that a slight rise in relative humidity (85 to 90 percent) caused a 20-percent dye loss in nylon fibers.

Both the type of dye and the material in which it is incorporated are important factors in the resistance a fabric has to ozone. Haynie et al. (1976) and Upham et al. (1976) found no effects from ozone concentrations of 0.1 to 0.5 ppm for 250 to 1000 hr under high and low relative humidity (90 versus 50 percent) on royal blue rayon-acetate, red rayon-acetate, or plum cotton. On the other hand, Haylock and Rush (1976, 1978) showed that anthraquinone dyes on nylon fibers were sensitive to fading from ozone at a concentration of 0.2 ppm at 70 percent relative humidity and 40°C for 16 hr. Moreover, the same degree of fading occurred in only 4 hr at 90 percent relative humidity. At higher concentrations, there was a parallel increase in fading. Along with Huevel et al. (1978) and Salvin (1969), Haylock and Rush (1976, 1978) noted the importance of surface area in relation to the degree of fading. In explaining this relationship, Kamath et al. (1982) found that ozone penetrated into the fiber itself and caused most of the fading through subsequent diffusion to the surface.

Field studies by Nipe (1981) and laboratory work by Kamath et al. (1982) showed a positive association between ozone levels and dye fading of nylon materials at an ozone concentration of 0.2 ppm and at various relative humidities. In summary, dye fading is a complex function of ozone concentration, relative humidity, and the presence of other gaseous pollutants. At present, the available research is insufficient for quantifying the amount of damage to fibrous materials attributable to ozone alone. Anthraquinone dyes incorporated into cotton and nylon fibers appear to be the most sensitive to ozone damage.

The degradation of fibers from exposure to ozone is poorly characterized. In general, most synthetic fibers such as modacrylic and polyester are relatively resistant; and cotton, nylon, and acrylic fibers show variable sensitivities to the gas. Ozone reduces the breaking strength of these fibers, and the degree of reduction depends on the amount of moisture present. Under laboratory conditions, Bogaty et al. (1952) found a 20 percent loss in breaking strength in cotton textiles under high-moisture conditions after exposure to a

0.06 ppm concentration of ozone for 50 days. They equated these conditions to a 500- to 600-day exposure under natural conditions. Kerr et al. (1969) found a net loss of 9 percent in breaking strength of moist cotton fibers exposed to ozone at a concentration of 1.0 ppm for 60 days. The limited research in this area indicates that ozone in ambient air may have a minimal effect on textile fibers, but additional research is needed to verify this conclusion.

1.8.2.3 Paints. The effects of ozone on paint are small in comparison with those of other factors (Campbell et al., 1974). Past studies have shown that, of various paints, only vinyl and acrylic coil coatings are affected (Haynie et al., 1976), and that this impact has a negligible effect on the useful life of the material coated. Preliminary results of current studies have indicated a statistically significant effect of ozone and relative humidity on latex house paint, but final results are needed before conclusions can be drawn.

Pigments in artists' paints have also been tested under controlled conditions for 3 months at an average exposure level of 0.4 ppm of ozone. While fading occurred in anthraquinone-based pigments, no quantitative information on dose-response relationships is available.

1.8.3 Economic Assessment of Effects of Ozone or Oxidants on Materials

Damage to nonbiological materials from ozone is usually expressed in terms of one or both of the following two general classes of costs to producers and consumers: (1) ozone accelerated replacement and repair costs, as when the service life and/or aesthetics of a material are impaired; and (2) increased avoidance costs, as when certain industries (e.g., manufacturers of tires, plastics, paints, dyes, and fabrics) are obligated to incur expenditures for antiozonant research and development, substitute processes and materials, additives and formulations, product packaging, advertising, etc., in order to offset sales losses that would otherwise occur.

In theory, the approach selected should depend on the observed behavior of the producers and consumers of the materials in question, and the type of damage to which they are reacting. In practice, the existing empirical estimates of ozone damage to materials are far from reliable for the reasons presented in the following paragraphs:

First, in some studies, coverage is limited to one or two classes of materials, and to restricted geographical regions. Other studies are entirely too aggregative, suffering deficiencies because of (1) broad and vague notions of materials exposure and ozone concentrations; (2) little or no data on the spatial and temporal distributions of the exposed materials; (3) unverified guesses regarding the incidence and level of cost increases and production adjustments incurred by ozone-affected industries; and (4) inadequate attention to economic trade-offs among different industries and different regions, and between producers versus consumers.

Second, the engineering and economic estimates are not well related to the scientific literature in this area, and tend to be far too simplistic to meet the concerns of the scientist. Third, most of the cost assessments were conducted in the early 1970s. Few recent studies exist. Moreover, these earlier studies cite extensively from each other and there are few independent analyses that do not merely rework old data.

As a consequence of the third item above, many of the ozone-related costs reported in the early 1970s for research and development, product substitution, etc., are no longer appropriate. Some of these were presumably once-only costs that are no longer charged against current production. Because the literature is dated, there may also be some current research and development and substitution attempts that are not reflected at all in the studies cited in Chapter 9. In addition, studies are outdated because the supply-demand relationships that prevailed when the studies were conducted may no longer be valid. In sum, the cost estimates largely reflect technologies, ozone or oxidant concentrations, and economic conditions that prevailed some 10 to 20 years ago.

Finally, most of the so-called economic studies of ozone damage to materials have been conducted using an engineering approach. That approach focuses on the classification and quantification of the various kinds of costs incurred by the producers and users of the ozone-sensitive materials. Economic theory would argue, however, that this is merely the first step in the assessment process, and that supply-demand relationships are then needed in order to proceed with the calculation of social net benefits (i.e., changes in producer and consumer surpluses). In practice, however, it appears that almost all of the damage assessments conducted to date stop short of obtaining an econometric measure of economic surplus. As such, the studies reported in Chapter 9 of this document must be interpreted accordingly.

Despite the shortcomings of the quantitative economic assessments that are available, the data indicate that, among the various materials studied, those most likely to affect the economy as the result of ozone exposure include elastomers and textile fibers and dyes. Among these, natural rubber used for tires is probably the most important economically for the following reasons: (1) significant ambient air exposure and long use life; (2) significant unit cost; and (3) large quantities and widespread distribution. McCarthy et al. (1983) calculated the cost of antiozonants in automobile and truck tires for protection against ozone. While limitations in this study preclude the reliable estimation of damage costs, the figures ($163 million in 1984 dollars) indicate the magnitude of potential damage from exposure to ozone in ambient air. Research has shown that house paint and certain textile fibers and dyes are also damaged by ozone; but the absence of reliable damage functions makes accurate economic assessments impossible. Thus, while damage to these materials is undoubtedly occurring, the actual damage costs cannot be estimated confidently.

1.9 INTRODUCTION TO HEALTH EFFECTS

The purpose of the health effects of chapters of this document is to describe the known biomedical effects of ambient levels of O_3 and other photochemical oxidants. Reports of animal, clinical, and epidemiological research are available for this purpose. They are reviewed in the following sections of this chapter. The primary goal of the review process is to describe and assess concentration-response relationships, particularly for concentrations at or near those found in ambient air, for both humans and laboratory animals. Such information is integral to the standard-setting process.

1.9.1 Organization of Health Effects Information

Reasons for the inclusion in this criteria document of Chapters 10 through 13 may not be self-evident to those who have never been involved in the preparation or review of criteria documents. Thus, the basic reasons are briefly noted below:

1. Chapter 10: Toxicologic Effects of Ozone and Other Photochemical Oxidants. *In vitro* studies on isolated cells and tissues and *in vivo* studies on laboratory animals permit the measurement of effects under circumstances that are not permissible in clinical research. Such studies in animals are useful for identifying mechanisms of effects; for determining concentration-response relationships over a wide range; for studying responses that require invasive procedures, such as tissue sampling and surgery; and for sorting out and testing hypotheses as a prelude to clinical investigations and as an aid in

the design of epidemiological studies. This information can be used to understand possible linkages between acute and chronic effects; and correlations of biochemical, functional and structural changes with growth, development and aging of the lung as the result of exposure to ozone. The chief weakness of animals studies lies in the difficulties and associated uncertainties of extrapolating results to humans.

2. Chapter 11: Controlled Human Studies - Studies on humans provide information about sensitive populations, dose-response relationships and responses to a limited number of repeated exposures. Such studies are necessarily restricted to ethically and legally acceptable pollutant concentrations and exposure regimes, as well as restricted to techniques for measurement of effects that are similarly constrained. The emphasis in human studies found in the literature is, therefore, on pulmonary function, with less on clearance, resistance to infection and even less on cytological effects. The chief weaknesses of controlled human exposure studies are: (a) small sample size; (b) the necessary absence of chronic exposure studies; (c) limitations on the range of pollutant concentrations and type of subjects studied; and (d) use of synthetic, simplified atmospheres, usually at unvarying concentrations, and usually without the changes in temperature, humidity, and pressure that occur in ambient conditions. The latter (d) also constitutes a strength of such studies, however, since it permits determination of concentration-response functions relative to a specific pollutant and specific end points.

3. Chapter 12: Field and Epidemiological Studies of the Effects of Ozone and Other Photochemical Oxidants - Epidemiological studies attempt to associate various characteristics of human health and function with ambient air concentrations of photochemical oxidants. Epidemiology involves the study of real-world human populations in their normal setting; of human responses to short-term and long-term oxidant exposure; and of sensitive subgroups within the population. Investigations within the normal setting are not, of course, without their drawbacks. The information gathered on exposure-effect relations and results may be confounded by the presence of factors such

as variations in the time spent out of doors, variations in activity levels, cigarette smoking, poor hygiene, coexisting pollutants, and socioeconomic status. Nevertheless, associations (or lack of them) can be drawn between health indicators and oxidant exposure. These associations may complement or extend the findings of clinical and toxicological research.

4. Chapter 13: Evaluation of Integrated Health Effects Data for Ozone and Other Photochemical Oxidants - The extensive body of data on the effects of ozone on the respiratory system was reported and discussed in particular detail in Chapters 10, 11, and 12. Chapter 13 provides a vehicle for evaluating this collective body of data for its significance to public health and for assessing the certainties and uncertainties associated with the data. Since the purpose of a criteria document is to provide a scientific basis for the derivation and promulgation of standards, this chapter also addresses specific issues and questions that are important in standard-setting. Paramount among the issues considered in standard-setting is the identification of the population or subpopulation to be protected by the regulation, that is, one that is at particular risk from exposure to ozone and other photochemical oxidants. The identification of such a population or subpopulation presupposes the identification of one or more effects that are in and of themselves adverse, or that are indicators of other effects that are adverse but that not measurable in man because of ethical constraints.

Three issues are not broached at all in the health effects chapters, inasmuch as they are regulatory issues that by law rest with the Administrator and by precedent are addressed for the Administrator by the Agency's Office of Air Quality Planning and Standards. These issues are: (1) determination of what constitues an "adverse effect;" (2) assessment of risk; and (3) determination of a margin of safety. While scientific data contribute significantly to decisions regarding them, the resolution of these issues cannot be achieved solely on the basis of experimentally acquired scientific information. Consequently, these issues are among the more problematic or difficult concepts and issues involved in protecting the public from the untoward effects of exposure to air pollutants.

1.9.2 Literature Coverage and Selection

The number of scientific reports on the biomedical effects of photochemical oxidants has grown substantially in recent years. To provide a comprehensive yet manageable review to satisfy the objectives of the criteria document, the most pertinent references must be identified for in-depth examination. Guidelines were developed to facilitate this process.

The material selected for review and comment in the text generally comes from the more recent literature, with emphasis on studies conducted at or near pollutant concentrations found in ambient air. Older literature that was cited in the previous criteria document for ozone and other photochemical oxidants (U.S. Environmental Protection Agency, 1978) has often been summarized and presented briefly. An attempt has been made, however, to discuss at greater length in the text older studies (1) judged significant because of their usefulness in deriving the 1979 standards; (2) open to reinterpretation because of newer data; or (3) potentially useful in deriving subsequent standards. The newer information on oxidants now available may in some instances make possible a better understanding of the earlier studies, such that a more detailed and comprehensive picture of health effects is emerging on several issues. An attempt has been made to discuss key literature in the text and present it in tables as well. Reports of lesser importance to the purposes of this document may appear in tables only.

Generally, only published material that has undergone scientific peer review is included. In the interest of admitting new and important information, however, the health effects chapters may also include some other materials that is thought to meet the standards of scientific reporting.

Studies cited in the chapters on toxicologic (Chapter 10) and clinical research (Chapter 11) are generally confined to those employing ozone at concentrations of 1 ppm or less. This concentration cutoff was chosen because ozone concentrations in ambient air rarely exceed 0.4 ppm (averaged over 1 hour) and then in only a few urban areas on rare occasions (Chapter 6). Typically, 1-hr maximum ozone levels are well below 0.2 ppm. Application of the concentration cutoff of 1 ppm eliminates discussions of studies on mortality and sublethal effects. Higher concentrations are cited, however, when (1) they have been used to extend the range of concentration-response relationships, as in multiple-concentration studies; (2) they elucidate mechanisms of effect; or (3) their use has resulted in the discovery of previously unreported effects.

In selecting studies for consideration, each paper was reviewed in detail. Technical considerations for inclusion of a specific study included, but were not restricted to, an analysis of the exposure method; specificity or appropriateness of the analytical method used to monitor the oxidant concentration; information on oxidant monitoring practices such as location, calibration, and sampling time; characteristics of the subjects; techniques used for obtaining cohorts; and the appropriateness of the technique used to measure the effect. Interpretation of the results included consideration of the following factors: the end results of the statistical analysis; the degree to which the results are plausible in the context of other extant data; the appropriateness of the hypothesis developed; and the agreement between the hypothesis and the results reported. No additional statistical analyses beyond those reported by the authors have been undertaken. Unless otherwise stated, all statements in the text, positive or negative, are statistically significant at $p < 0.05$ or less.

1.10 TOXICOLOGIC EFFECTS OF OZONE AND OTHER PHOTOCHEMICAL OXIDANTS

1.10.1 Introduction

The biological effects of ozone have been studied extensively in animals and a wide array of toxic effects has been ascribed to ozone inhalation. Although much has been accomplished to improve the existing data, refine the concentration-response relationships, and better interpret the mechanisms of ozone effects, many of the present data were not accumulated for the purpose of making quantitative comparisons across animal studies or deriving concentration-response functions. In many cases, only qualitative comparisons can be made. To maximize the extent that animal toxicological data can be used to estimate the human health risk of exposure to ozone, the qualitative as well as quantitative similarities between the toxicity of ozone to animals and to man must be considered. Significant advances have been made in understanding the toxicity of ozone through appropriate animal models. This summary highlights the results of selected studies that will provide data useful for predicting and assessing, in a scientifically sound manner, possible human responses to ozone.

Summary figures and tables are presented in the following sections. Studies were selected for inclusion in these figures and tables on the basis of specific criteria presented below:

1. Studies have been cited only if the reported effects are clearly due to O_3 exposure. Studies involving mixtures of O_3 and other pollutants or those involving exercise, diet deficiencies, or other possible modifiers of response to O_3 have not been included.
2. Cited studies report the effects of O_3 exposure over a broad range of animal species and strains and for varying lengths of time. Specific details on animal species, exposure duration, and observed effects can be obtained from the tables in Chapter 10.
3. Each closed symbol on the figures represents one or more studies conducted at that particular concentration. Specific responses can be found in the accompanying tables.
4. Only pulmonary function effects were divided by short-term (<14 days) and long-term (>14 days) exposures to follow the discussion in the text.

1.10.2 Respiratory Transport and Absorption of Ozone

The respiratory system is the route of entry for ozone and other oxidizing air pollutants, just as it is for air itself. Throughout inhalation and exhalation, ozone undergoes transfer from the gas phase to the airway surfaces and parenchyma. Not all of the gas is taken up, however; a variable fraction is expelled with exhalation. Following contact with the respiratory tract, ozone or its transformation products can react with both extra- and intracellular elements.

The amount of ozone acting at a given site in the lung is related to the airway luminal concentration at that level. Thus, ozone does not immediately interact with cellular components of the respiratory tract. Instead, it first comes into contact with the mucous or surfactant layer lining the airway. It should be noted here that ozone is quite reactive chemically. Reactions with components of this layer result in an increase in total absorption of ozone in the upper airways and reduces the amount of ozone reaching sensitive tissues. The site at which uptake and subsequent interaction occur and the local dose (quantity of ozone absorbed per unit area), along with cellular sensitivity, will determine the type and extent of the injury. For this reason, a thorough knowledge of the complex process of gas transport and absorption within the respiratory tract is crucial to understanding the effects of ozone and other oxidants in humans.

Measurements of the regional uptake of ozone and other oxidants that are reactive and metabolized by body tissue and fluids are just beginning. Comparative uptake studies between man and animals have not yet appeared in the literature. Studies with aerosols, however, have shown similarities in deposition in both the total respiratory tract and in the pulmonary region in guinea pig, rabbit, rat, and man. Nevertheless, some interspecies differences, especially in regional deposition and uptake, may be expected. Such differences may be imposed by modes of breathing. For example, rodents breathe only by nose, while humans may breathe nasally, oronasally, or orally, depending on a variety of factors. Differences may also result from differences among species in anatomic and morphometric structures. For example, respiratory bronchioles are absent or primordial in rats, but are well developed in primates. Similarly, the capacity for responding to a specific dose may vary between animals and humans because of dissimilarities in detoxification systems, pharmacokinetics, metabolic rates, genetic makeup, or other factors. Such differences must be accounted for when extrapolating the results of animal studies to the human population.

The animal studies that have been conducted are beginning to indicate the quantity and site of ozone uptake in the respiratory tract. For example, experiments conducted to determine the nasopharyngeal removal of ozone in animals have demonstrated (1) that the fraction of ozone taken up is inversely related to the flow rate and ozone concentration, (2) that uptake is greater for nose than for mouth breathing, and (3) that tracheal and exposure chamber concentrations are positively correlated (Yokoyama and Frank, 1972; Moorman et al., 1973; Miller et al., 1979). The limited data available indicate that at concentrations of ozone ranging from 0.1 to 2.0 ppm, removal of ozone in the nasopharyngeal region would be expected to be approximately 50 percent of the inhaled ozone.

Morphological studies have provided substantiating data that ozone is absorbed along the entire respiratory tract, penetrating further into the peripheral nonciliated airways and the respiratory bronchioles as inhaled ozone concentration increases from 0.2 ppm to 0.8 ppm (Dungworth et al., 1975). From animal studies, it has been predicted that in man, rabbit, and guinea pig the pattern of ozone deposition is similar, with one specific area of the lung, the junction of the conducting airways and the gas-exchange region, receiving the maximal dose (Miller et al., 1978). This prediction correlates well with reported histopathological data of Dungworth et al. (1975) and Stephens et al. (1974).

To date, there has been only one study (Yokoyama and Frank, 1972) that attempted to measure ozone uptake in the lower respiratory tract. These data indicate that in dogs, 80 to 87 percent of the inhaled ozone was taken up by the lower respiratory tract. It should be noted that this estimates the uptake as applied to the total lung and does not describe the uptake of ozone by individual airways or airway generations.

Three models appear to have merit for estimating ozone uptake in the respiratory tract (Aharonson et al., 1974; McJilton et al., 1972; Miller et al., 1978).

The model of Aharonson et al. (1974) is useful in analyzing nasopharygeal uptake data. Applied to ozone data, the model indicates that the average mass transfer coefficient is the nasopharygeal region increases with increasing air flow.

The McJilton model (McJilton et al., 1972) and the Miller model (Miller et al., 1978) for lower respiratory tract ozone uptake are similar in their treatment of ozone in the airways, taking into account convection, diffusion, wall losses, and ventilatory patterns; and in their use of morphological data for defining the dimensions of the airways and their liquid lining. The Miller model is more realistic, however, because it accounts for chemical reactions of ozone with constituents of the mucous-serous layer. Tissue dose is predicted by the Miller model to be relatively low in the trachea, to increase to a maximum between the junction of the conducting airways and the gas-exchange region, and then to decrease distally. Comparison of the Miller results with morphological data indicates qualitative agreement in the pulmonary region. Comparison in the tracheobronchial region indicates, however, that further research is needed to define the relevant toxic chemical and physical mechanisms.

Ozone dosimetry modeling is in its formative stages, and at present there are few experimental results that are useful for judging the validity of the modeling efforts. With experimental confirmation, models can become practical tools for understanding respiratory tract transport and absorption of ozone and for understanding ozone dosimetry in respective species.

1.10.3 Effects of Ozone on the Respiratory Tract

1.10.3.1 Morphological Effects. Morphological studies of the effects of ozone have indicated that the pattern and distribution of tissue lesions are similar in the respective species studied. They depend, however, upon (1) the location of the sensitive cells and (2) the location of the junction between the conducting airways and the gas-exchange region of the lung, both of which are species-specific. Damage to all parts of the respiratory tract can occur in animals, depending on the ozone concentration. At low concentrations of ozone (< 1960 μg/m^3; 1 ppm), damage is principally confined to the junction between the alveoli and the conducting airways. Dogs, monkeys, and man have respiratory and nonrespiratory bronchioles, while respiratory bronchioles are either absent or poorly developed in mice, rats, and guinea pigs. The location of the ozone lesion thus differs according to the species examined (Plopper et al., 1979; Castleman et al., 1977, 1980; Dungworth et al., 1975a; Eustis et al., 1981). In both types of lungs, the effects of ozone have been found at concentrations as low as 392 μg/m^3 (0.2 ppm) and for exposure times as short as 2 hr (Stephens et al., 1974a).

In the upper and lower conducting airways, ciliated cells appear to be the most sensitive cell type; they are damaged by exposures to ozone at concentrations as low as 392 to 1568 μg/m^3 (0.2 to 0.8 ppm) for 8 or 24 hr for 7 days in rats (Schwartz et al., 1976), bonnet monkeys (Castleman et al., 1977), Rhesus monkeys (Dungworth et al., 1975b; Mellick et al., 1977), and mice (Ibrahim et al., 1980). When Moore and Schwartz (1981) and Boorman et al. (1980) extended these exposures to 180 days at the same concentrations, similar changes in these ciliated cells were observed. Uniform damage was not always noted; most often shortened and less dense cilia occurring in random patches were reported. Electron microscopy revealed severe cytoplasmic changes and condensed nuclei. Damage is present in both trachea and bronchi (Eustis et al., 1981; Mellick et al., 1977; Castleman et al., 1977). The damaged cilia are replaced by nonciliated clara cells that become hyperplasic (Evans et al., 1976a; Lum et al., 1978).

In mice, ozone levels of 980 and 1568 μg/m^3 (0.5 and 0.8 ppm) elicited a pronounced hyperplasia of these nonciliated cells that persisted for 10 days after cessation of the exposure (Zitnik et al., 1978; Ibrahim et al., 1980). In a number of species, ozone damage is clearly evident at the centriacinar region, which includes the terminal bronchiole region, portions of the respiratory bronchioles, and possibly the alveolar ducts, depending on the species (Stephens et al., 1973, 1974a,b; Schwartz et al., 1976; Mellick et al., 1977).

Type 1 epithelial cells are significantly affected (Stephens et al., 1974a; Evans et al., 1976a; Castleman et al., 1980; Eustis et al., 1981; Barry et al., 1983; Boorman et al., 1980). In monkeys, for example, at 1764 μg/m^3 (0.9 ppm), death of type 1 cells reaches a maximum at 12 hr after continuous exposure (Castleman et al., 1980). With the destruction of these cells, there is a hyperplasia of type 2 alveolar epithelial cells, which re-covers the denuded basal lamina (Stephens et al., 1974a,b; Sherwin et al., 1983; Eustis et al., 1981). Type 2 cells are relatively resistant to ozone exposure.

Following and during continued exposures, these type 2 cells begin to proliferate, which is a hallmark of ozone injury regardless of species. In rats, DNA synthesis in type 2 cells was reported as early as 4 hr after exposure to O_3 to 392 $\mu g/m^3$ (0.2 ppm) (Stephens et al., 1974a) and reached a maximum at 2 days following continuous exposure to 686 or 980 $\mu g/m^3$ (0.35 or 0.5 ppm) (Evans et al., 1976a,b), or 1568 $\mu g/m^3$ (0.8 ppm) (Boorman et al., 1980). Although type 2 cells proliferated in the ozone-exposed lung, complete maturation of type 2 cells to type 1 cells did not occur, even as late as 180 days of exposure (Moore and Schwartz, 1981). In the normal progression, type 2 cells would have matured into type 1 cells. Continued ozone exposure inhibits both ciliagenesis and type 2 cell maturation.

Inflammation occurs in all species examined so far. The inflammatory response is seen as early as 4 hr after exposure to 1568 $\mu g/m^3$ (0.8 ppm) in monkeys (Castleman et al., 1980). In rats and monkeys, inflammation persists with continued exposure, although at reduced levels. The inflammatory exudate includes both fibrin and various leukocytes in the initial phase. In the later phase the inflammatory cells are predominantly macrophages (Castleman et al., 1980; Brummer et al., 1977; Boorman et al., 1980; Moore and Schwartz, 1981). Quantitative estimates of the degree of inflammation are, however, lacking at present. The contribution of the inflammatory response to subsequent long-term features of ozone toxicity has not been studied in detail, even though techniques are available. A number of studies have reported that exposure to 980 $\mu g/m^3$ (0.5 ppm) and above thickens the interalveolar septa of centriacinar alveoli (Schwartz et al., 1976; Castleman et al., 1980; Boorman et al., 1980). Thickness could be caused by interstitial fibrosis.

Although some delay has been observed between an exposure to ozone and the maximum manifestation of morphological changes, the shortest time required for ozone exposure to result in significant morphological changes is 2 hr, at 392 or 980 $\mu g/m^3$ (0.2 or 0.5 ppm) in rats (Stephens et al., 1973, 1974a,b) or 4.7 or 6.6 hr of exposure by endotracheal tube in cats to 510, 980, or 1960 $\mu g/m^3$ (0.26, 0.5, or 1 ppm) (Boatman et al., 1974). Most of these morphological studies were specifically designed, however, to look at long-term (i.e., days, months, years) exposures rather than acute effects. The data from acute studies are in agreement with molecular theories that ozone acts rapidly to oxidize some critical tissue component. Little difference in severity was noted by Schwartz et al. (1976) between exposure to 8 hr/day or 24 hr/day when the exposure was continued for 7 days. Quantitative studies of different exposure regimens are lacking but are technically feasible. The sequence in which the anatomic sites are affected appears to be a function of concentration rather than of exposure duration. Increasing the concentrations of ozone not only results in more severe lesions, but also extends the lesion to higher generations of the respiratory structure.

Morphological studies of vitamin E-deficient or supplemented rats have been undertaken to correlate the biochemical findings with morphological alterations (Plopper et al., 1979; Stephens et al., 1983; Chow et al., 1981; Schwartz et al., 1976; Sato et al., 1976a,b, 1978, 1980). Despite the presence of vitamin E in the diets of these animals, however, the morphological lesion resulting from ozone exposure was unchanged.

When comparisons are made at analogous anatomical sites, the morphological effects of ozone on the lungs of a number of species of animals are seen to be remarkably similar. Despite the inherent differences in anatomy between most experimental animals and man, the junction between the conducting airways and the gas exchange region is the site affected most by ozone.

Studies on the morphologic effects of ozone exposures of experimental animals are summarized in Figure 1-9 and Table 1-12 (see Section 1.10.1 for criteria used to summarize the studies).

1.10.3.2 Pulmonary Function. One of the limitations of animal studies is that many pulmonary function tests comparable to those conducted after acute exposure of human subjects are difficult to interpret. Methods exist, however, for obtaining similar measurements of many variables pertinent to understanding the effects of ozone on the respiratory tract, particularly after longer exposure periods. A number of newer studies reported here reflects recent advances in studying pulmonary function in small animals.

Changes in lung function following ozone exposure have been studied in mice, rats, guinea pigs, rabbits, cats, dogs, sheep, and monkeys. Short-term exposure for 2 hr to concentrations of 431 to 980 $\mu g/m^3$ (0.22 to 0.5 ppm) produces rapid, shallow breathing and increased pulmonary resistance during exposure (Murphy et al., 1964; Yokoyama, 1969; Watanabe et al., 1973; Amdur et al., 1978). The onset of these effects is rapid and the abnormal breathing pattern usually disappears within 30 min after cessation of exposure. Other changes in lung function measured following short-term ozone exposures lasting

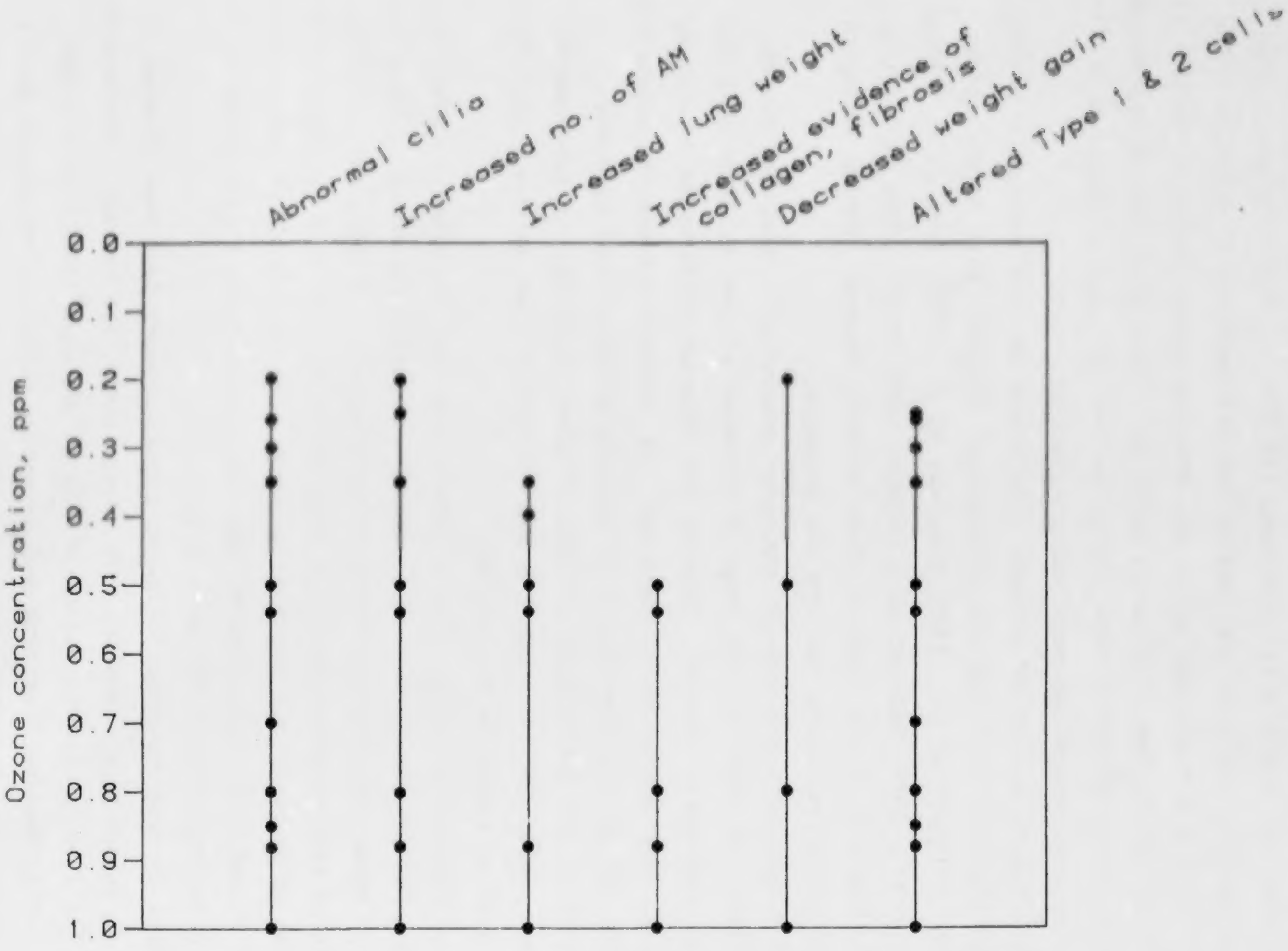

Figure 1-9. Summary of morphological effects in experimental animals exposed to ozone. See Table 1-12 for reference citations for studies summarized here.

TABLE 1-12. MORPHOLOGICAL EFFECTS OF OZONE IN EXPERIMENTAL ANIMALS

Effect/response	O_3 concentration, ppm	References
Abnormal cilia	0.2, 0.35, 0.5, 0.8	Dungworth et al. (1975b)
	0.2	Plopper et al. (1979)
	0.2, 0.35	Castleman et al. (1977)
	0.2, 0.5, 0.8	Schwartz et al. (1976)
	0.8	Boorman et al. (1980)
	0.26, 0.5, 1.0	Boatman et al. (1974)
	0.3	Sato et al. (1976a)
	0.5, 0.8	Eustis et al. (1981)
	0.5, 0.8	Mellick et al. (1975, 1977)
	0.54, 0.88	Stephens et al. (1974a)
	0.7	Evans et al. (1976a)
	0.8	Ibrahim et al. (1980)
	0.8	Lum et al. (1978)
	0.8	Plopper et al. (1978)
	0.85	Stephens et al. (1978)
Increased number of alveolar macrophages (AM)	0.2	Plopper et al. (1979)
	0.2, 0.35, 0.5, 0.8	Dungworth et al. (1975b)
	0.2, 0.35	Castleman et al. (1977)
	0.2, 0.5, 0.8	Boorman et al. (1977, 1980)
	0.25	Barry et al. (1983)
	0.5	Zitnik et al. (1978)
	0.5, 0.88	Stephens et al. (1974a)
	0.5	Last et al. (1979)
	0.54, 0.88	Freeman et al. (1974)
	0.8	Castleman et al. (1980)
	1.0	Freeman et al. (1973)
	1.0	Cavender et al. (1977)
	0.5, 0.88	Brummer et al. (1977)
	0.5, 0.8	Eustis et al. (1981)
	0.2	Dungworth (1976)
	0.2	Stephens et al. (1976)
Increased evidence of collagen, fibrosis	0.5, 0.8	Last et al. (1979)
	0.54, 0.88	Freeman et al. (1974)
	1.0	Stokinger et al. (1957)
	1.0	Freeman et al. (1973)
Increased lung weight, edema	0.5, 1.0	Fukase et al. (1978)
	0.54, 0.88	Freeman et al. (1974)
	1.0	Cavender et al. (1977)
	0.4	P'an et al. (1972)
	0.35	Castleman et al. (1977)

TABLE 1-12. MORPHOLOGICAL EFFECTS OF OZONE IN EXPERIMENTAL ANIMALS (continued)

Effect/response	O_3 concentration, ppm	References
Decreased weight gain	0.2, 0.5, 0.8	Schwartz et. al. (1976)
	0.5, 1.0	Fukase et al. (1978)
Altered type 1 and 2 cells	0.25	Barry et al. (1983)
	0.26, 0.5, 1.0	Boatman et al. (1974)
	0.3	Sherwin et al. (1983)
	0.35, 0.5, 0.7, 1.0	Evans et al. (1976b)
	0.5	Stephens et al. (1974b)
	0.5	Zitnik et al. (1978)
	0.5, 0.8	Eustis et al. (1981)
	0.54, 0.88	Stephens et al. (1974a)
	0.5, 0.8	Mellick et al. (1975, 1977)
	0.5, 1.0	Cavender et al. (1977)
	0.54, 0.88	Freeman et al. (1974)
	0.7, 0.8	Castleman et al. (1973, (1980)
	0.8	Plopper et al. (1978)
	0.85	Stephens et al. (1978)

3 hr to 14 days are usually greatest 1 day following exposure and disappear by 7 to 14 days following exposure. These effects are associated with premature closure of the small, peripheral airways and include increased residual volume, closing volume, and closing capacity (Inoue et al., 1979).

The effects of short-term exposures to ozone on pulmonary function and airway reactivity in experimental animals are summarized in Figure 1-10 and Table 1-13 (see Section 1.10.1 for criteria for selecting studies summarized).

Long-term exposure of 4 to 6 weeks to ozone concentrations of 392 to 490 µg/m^3 (0.2 to 0.25 ppm) increases lung distensibility at high lung volumes in young rats (Bartlett et al., 1974; Raub et al., 1983a). Similar increases in lung distensibility were found in older rats exposed to 784 to 1568 µg/m^3 (0.4 to 0.8 ppm) for up to 180 days (Moore and Schwartz, 1981; Costa et al., 1983; Martin et al., 1983). Three to twelve months of exposure to O_3 concentrations of 1176 to 1568 µg/m^3 (0.6 to 0.8 ppm) increased pulmonary resistance and caused impaired stability of the small peripheral airways in both rats and monkeys (Costa et al., 1983; Wegner, 1982). The effects in monkeys were not completely reversed by 3 months following exposure; lung distensibility had also decreased in the postexposure period, suggesting the development of lung fibrosis.

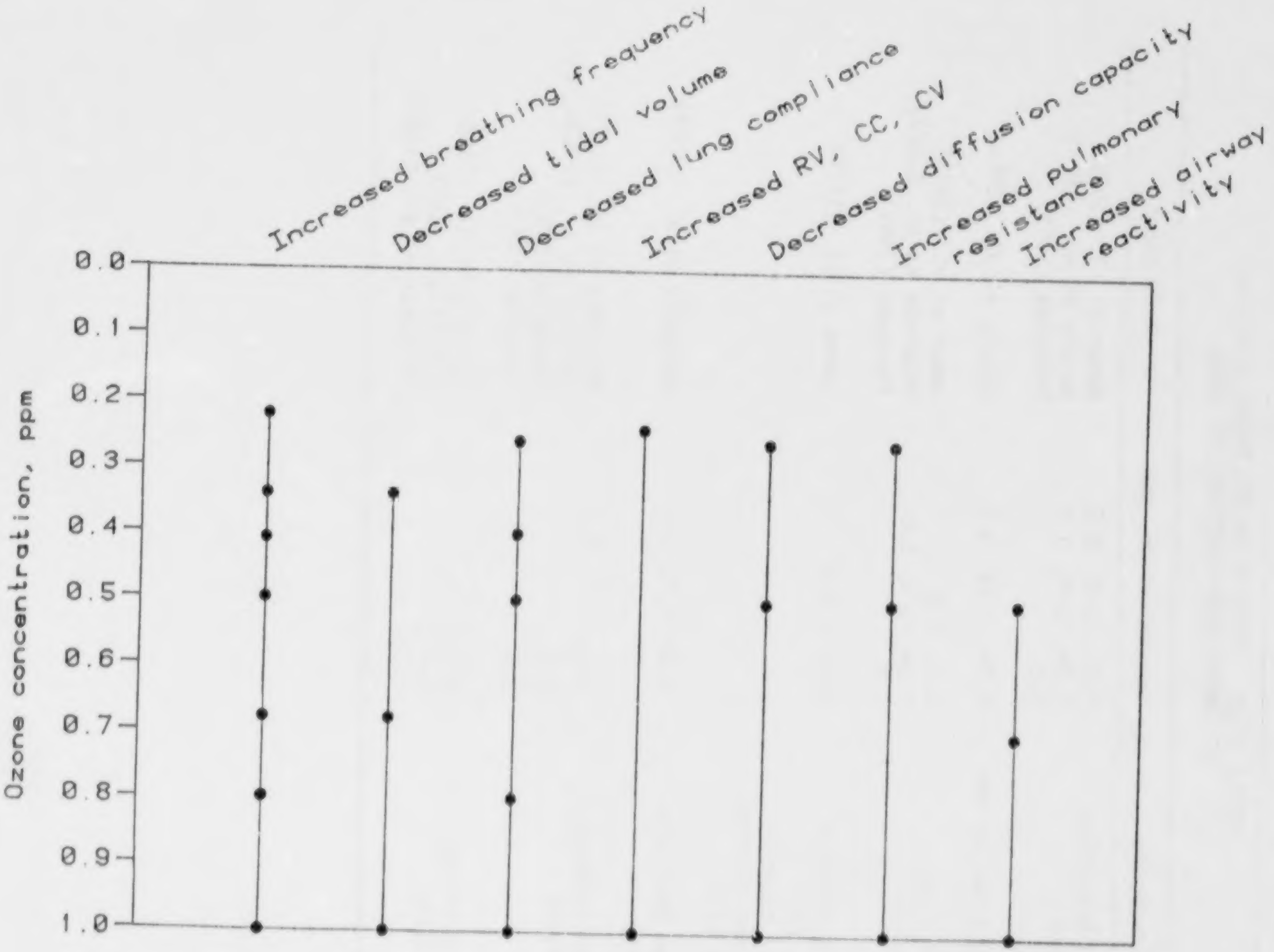

Figure 1-10. Summary of effects of short-term ozone exposures on pulmonary function in experimental animals. See Table 1-13 for reference citations for studies summarized here.

TABLE 1-13. EFFECTS ON PULMONARY FUNCTION OF SHORT-TERM EXPOSURES TO OZONE

Effect/response	O_3 concentration, ppm	References
Increased breathing frequency	0.22, 0.41, 0.8	Amdur et al. (1978)
	0.34, 0.68, 1.0	Murphy et al. (1964)
	0.5	Yokoyama (1969)
Decreased tidal volume	0.34, 0.68, 1.0	Murphy et al. (1964)
Decreased lung compliance	0.4, 0.8	Amdur et al. (1978)
	0.26, 0.5, 1.0	Watanabe et al. (1973)
	1.0	Yokoyama (1969)
Increased residual volume (RV), closing capacity (CC), and closing volume (CV)	0.24 - 1.0	Inoue et al. (1979)
Decreased diffusion capacity	0.26, 0.5, 1.0	Watanabe et al. (1973)
Increased pulmonary resistance	0.26, 0.5, 1.0	Watanabe et al. (1973)
	1.0	Gertner et al. (1983a, b)
	0.5	Yokoyama (1969)
	1.0	Yokoyama (1974)
Increased airway reactivity	0.5	Abraham et al. (1980)
	0.7	Lee et al. (1977)
	1.0	Holtzman et al. (1983)

The effects of long-term exposures to ozone on pulmonary function and airway reactivity in experimental animals are summarized in Figure 1-11 and Table 1-14 (see Section 1.10.1 for criteria for summary).

Studies of airway reactivity following ozone exposure in experimental animals show that ozone increases the reactivity of the lung to mechanical and chemical stimulation partly by increased sensory neural activity travelling in the vagus nerve and partly by a local action of ozone on the tissues. Aerosolized ovalbumin can reach immunologic receptors in the lungs of mice preexposed to 980 or 1568 $\mu g/m^3$ (0.5 or 0.8 ppm) continuously for 3 to 5 days (Osebold et al., 1980), resulting in an increased incidence of anaphylaxis. Increased sensitivity to histamine or cholinomimetic drugs by aerosol or injection has been noted in several species. Easton and Murphy (1967) showed that the lethal dose of histamine in guinea pigs was reduced in those animals preexposed to concentrations as low as 980 or 1960 $\mu g/m^3$ (0.5 or 1 ppm) of ozone for 2 hr. The pulmonary resistance due to subcutaneous injection of histamine increased in guinea pigs exposed to 1568 $\mu g/m^3$ (0.8 ppm) of ozone for 1 hr (Gordon and Amdur, 1980). Similarly, dogs exposed to 1372 and 1960 $\mu g/m^3$ (0.7 and 1.0 ppm) of ozone for 2 hr had greater changes in pulmonary resistance following histamine aerosol inhalation (Lee et al., 1977; Holtzman et al., 1983a). Sheep exposed to 980 $\mu g/m^3$ (0.5 ppm) of ozone for 2 hr experienced increased pulmonary resistance for the cholinomimetic drug, carbachol (Abraham et al., 1980).

The time course of ozone-induced airway hyperreactivity suggests a possible association with inflammation (Holtzman et al., 1983a,b; Sielczak et al., 1983; Fabbri et al., 1984), but responses are variable and not very well understood. Additional studies that demonstrate increased collateral resistance following 30-min local exposure of ozone or histamine in sublobar bronchi of dogs (Gertner et al., 1983a,b,c) suggest that other mechanisms, along with amplification of reflex pathways, may contribute to changes in airway reactivity.

1.10.3.3 Biochemical Effects of Ozone in the Lung of Experimental Animals. The lung is metabolically active, and several key steps in metabolism have been studied after O_3 exposure. Since the procedures for such studies are invasive, this research has been conducted only in animals. Effects, to be summarized below, have been observed on antioxidant metabolism, oxygen consumption, proteins, lipids, and xenobiotic metabolism.

The lung contains several compounds (e.g., vitamin E, sulfhydryls, glutathione) and enzymes (e.g., glutathione peroxidase, glutathione reductase,

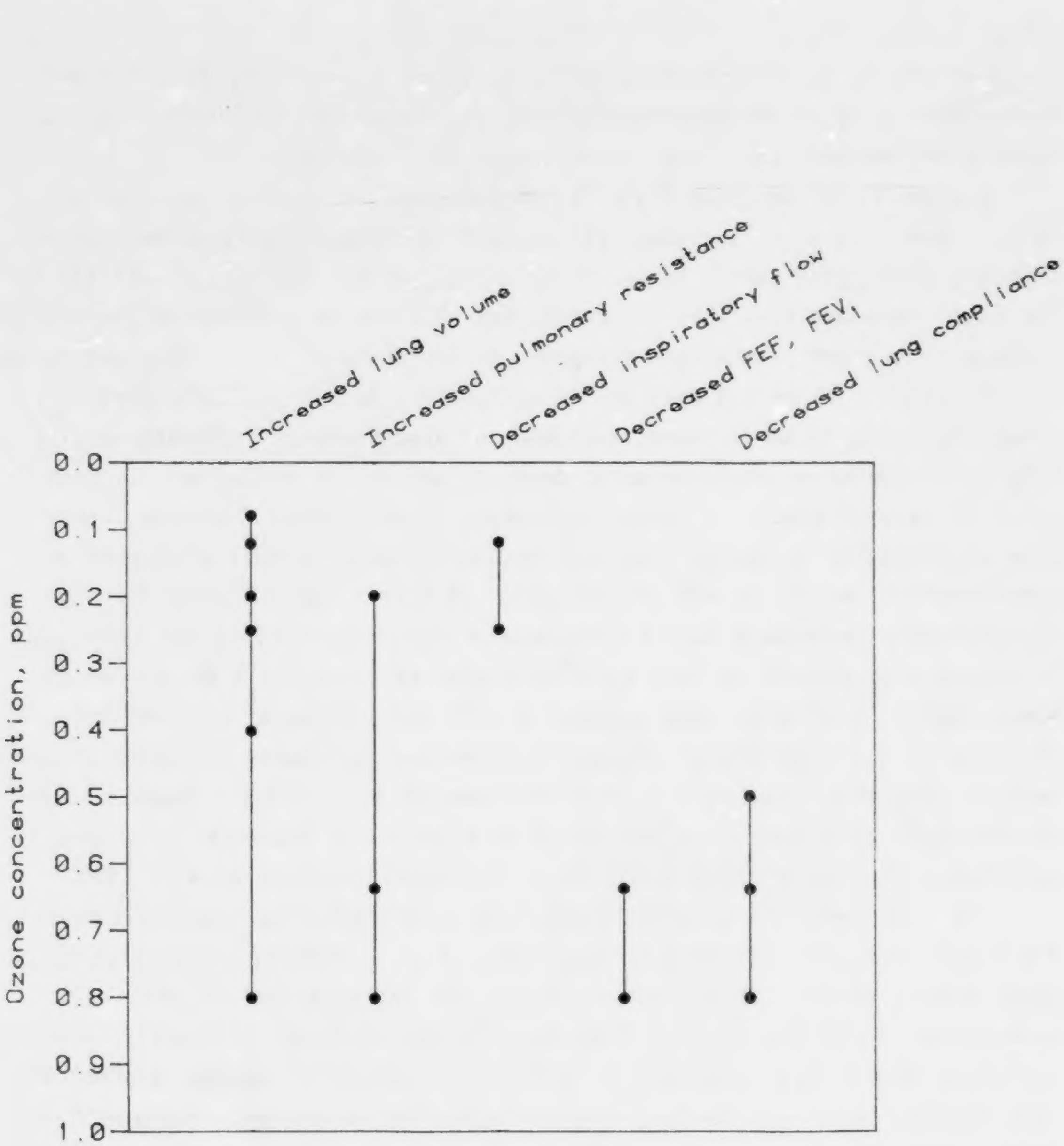

Figure 1-11. Summary of effects of long-term ozone exposures on pulmonary function in experimental animals. See Table 1-14 for reference citations for studies summarized here.

TABLE 1-14. EFFECTS ON PULMONARY FUNCTION OF LONG-TERM EXPOSURES TO OZONE

Effect/response	O_3 concentration, ppm	References
Increased lung volume	0.08, 0.12, 0.25 0.2 0.8 0.4	Raub et al. (1983) Bartlett et al. (1974) Costa et al. (1983) Martin et al. (1983)
Increased pulmonary resistance	0.2, 0.8 0.64	Costa et al. (1983) Wegner (1982)
Decreased lung compliance	0.5, 0.8 0.64	Eustis et al. (1981) Wegner (1982)
Decreased inspiratory flow	0.12, 0.25	Raub et al. (1983)
Decreased forced expiratory volume (FEV_1) and flow (FEF)	0.64 0.8	Wegner (1982) Costa et al. (1983)

glucose-6-phosphate dehydrogenase, and superoxide dismutase) that function as antioxidants, thereby defending the lung against oxidant toxicity from the oxygen in air, from oxidants produced during metabolic processes, and from oxidizing air pollutants such as ozone. Obviously, this protection is only partial for ozone since exposure to ozone causes numerous effects on lung structure, function, and biochemistry. Acute exposure to high ozone levels (2920 μg/m^3, 2 ppm) typically decreases antioxidant metabolism, whereas repeated exposures to lower levels ($\leq$ 1568 μg/m^3, 0.8 ppm) increases this metabolism (DeLucia et al., 1975). In rats maintained on normal diets, this response has been observed after a week of continuous or intermittent exposure to 392 μg/m^3 (0.2 ppm) O_3 (Mustafa, 1975; Mustafa and Lee, 1976; Plopper et al., 1979). Similar responses are seen in monkeys and mice, but at higher concentrations (980 μg/m^3, 0.5 ppm; Fukase et al., 1978; Mustafa and Lee, 1976).

The effects of ozone on oxygen consumption have been studied since oxygen consumption is a fundamental parameter of cellular metabolism, reflecting energy production by cells. As with antioxidant metabolism, acute exposure to high ozone levels ($\geq$ 3920 μg/m^3; $\geq$ 2 ppm) decreases metabolism (and thus, oxygen consumption); repeated exposure to lower levels (> 1568 μg/m^3, 0.8 ppm) increases oxygen consumption (Mustafa et al., 1973; Schwartz et al., 1976; Mustafa and Lee, 1976). Effects in rats on normal diets have been observed after a short-term exposure to ozone levels as low as 392 μg/m^3 (0.2 ppm) (Schwartz et al., 1976; Mustafa et al., 1973; Mustafa and Lee, 1976). Monkeys are affected at a higher level of ozone (980 μg/m^3, 0.5 ppm).

Similar patterns of response for both antioxidant metabolism and oxygen consumption are observed after exposure to ozone. A 7-day exposure to ozone produces linear concentration-related increases in activities of glutathione peroxidase, glutathione reductase, glucose-6-phosphate dehydrogenase, and succinate oxidase (Mustafa and Lee, 1976; Chow et al., 1974; Schwartz et al., 1976; Mustafa et al., 1973). Rats on a vitamin E-deficient diet experience an increase in enzyme activities at 196 μg/m^3 (0.1 ppm) ozone as compared to 392 μg/m^3 (0.2 ppm) in animals on normal diets (Chow et al., 1981; Mustafa and Lee, 1976; Mustafa, 1975). Research on these enzymes has shown that there is no significant difference in effects from continuous versus intermittent exposure; this, along with concentration-response data, suggests that the concentration of ozone is more important than duration of exposure in causing these effects (Chow et al., 1974; Schwartz et al., 1976; Mustafa and Lee, 1976).

Duration of exposure still plays a role, however. During exposures up to 1 or 4 weeks, antioxidant metabolism and O_2 consumption generally do not change on the first day of exposure; by about day 4 a plateau is reached (Mustafa and Lee, 1976; DeLucia et al., 1975). Recovery from these effects occurs by 6 days post-exposure (Chow et al., 1976). This apparent tolerance is not long-lasting. If rats are re-exposed after recovery is observed, the increase in enzyme activities is equivalent to that observed in animals exposed for the first time (Chow et al., 1976). The influence of age on responsiveness is also similar for antioxidant metabolism and oxygen consumption (Elsayed et al., 1982a; Tyson et al., 1982; Lunan et al., 1977). Suckling neonates (5 to 20 days old) generally exhibited a decrease in enzyme activities; as the animals grew older (up to about 180 days old), enzyme activities generally increased with age. Species differences may exist in this response (Mustafa and Lee, 1976; Mustafa et al., 1982; Chow et al., 1975; DeLucia et al., 1975). Studies in which monkeys have been compared to rats did not include, however, a description of appropriate statistical considerations applied (if any). Thus, no definitive conclusions about responsiveness of monkeys versus rats can be made.

The mechanism responsible for the increase in antioxidant metabolism and oxygen consumption is not known. The response is typically attributed, however, to concurrent morphological changes, principally the loss of type 1 cells and an increase in type 2 cells, which are rich in the enzymes measured.

Monooxygenases constitute another class of enzymes investigated after ozone exposure. These enzymes function in the metabolism of both endogenous (e.g., biogenic amines, hormones) and exogenous (xenobiotic) substances. The substrates acted upon are either activated or detoxified, depending on the substrate and the enzyme. Acute exposure to 1470 to 1960 $\mu g/m^3$ (0.75 to 1 ppm) ozone decreased cytochrome P-450 levels and enzyme activities related to both cytochrome P-450 and P-448. The health impact of these changes is uncertain since only a few elements of a complex metabolic system were measured.

The activity of lactate dehydrogenase is increased in lungs of vitamin E-deficient rats receiving a short-term exposure to 196 $\mu g/m^3$ (0.1 ppm) ozone (Chow et al., 1981). Higher levels caused a similar response in rats, but not in monkeys, on normal diets (Chow et al., 1974, 1977). This enzyme is frequently used as a marker of cellular damage because it is released upon cytotoxicity. It is not known, however, whether the increase in this enzyme is a direct reflection of cytotoxicity or whether it is an indicator of an increased number of type 2 cells and macrophages in the lungs.

An increase in a few of the measured activities of lysosomal enzymes has been shown in the lungs of rats exposed to $\geq$ 1372 $\mu g/m^3$ (0.7 ppm) ozone (Dillard et al., 1972; Castleman et al., 1973a; Chow et al., 1974). This response is most likely the result of an increase in inflammatory cells in the lungs rather than an induction of enzymes, since lysosomal enzymes in alveolar macrophages decrease after _in vivo_ or _in vitro_ exposure to ozone (Hurst et al., 1970; Hurst and Coffin, 1971).

As discussed previously, long-term exposure to high O_3 concentrations causes mild lung fibrosis (i.e., local increase of collagen in centriacinar interalveolar septa). This morphological change has been correlated with biochemical changes in the activity of prolyl hydroxylase (an enzyme that catalyzes the production of hydroxyproline) and in hydroxyproline content (a component of collagen that is present in excess in fibrosis) (Last et al., 1979; Bhatnagar et al., 1983). An increase in collagen synthesis has been observed, with 980 $\mu g/m^3$ (0.5 ppm) O_3 being the minimally effective concentration tested (Hussain et al., 1976a,b; Last et al., 1979). During a prolonged exposure, prolyl hydroxylase activity increases by day 7 and returns to control levels by 60 days of exposure. When a short-term exposure ceases, prolyl hydroxylase activity returns to normal by about 10 days post-exposure, but hydroxyproline levels remain elevated 28 days post-exposure. Thus, the product of the increased synthesis, collagen, remains relatively stable.

Although the ability of O_3 to initiate peroxidation of unsaturated fatty acids _in vitro_ is well established, few _in vivo_ studies of lung lipids have been conducted. Generally, ozone decreases unsaturated fatty acid content of the lungs (Roehm et al., 1972) and decreases incorporation of fatty acids into lecithin (a saturated fatty acid) (Kyei-Aboagye et al., 1973). These alterations, however, apparently do not alter the surface-tension-lowering properties of lung lipids that are important to breathing (Gardner et al., 1971; Huber et al., 1971).

One of the earliest demonstrated effects of ozone was that very high concentrations caused mortality as a result of pulmonary edema. As more sensitive techniques were developed, lower levels (510 $\mu g/m^3$, 0.26 ppm) were observed to increase the protein content of the lung (Hu et al., 1982). Since some of the excess protein could be attributed to serum proteins, the interpretation was that edema had occurred. This effect was more pronounced several hours after exposure ceased. At higher concentrations, a loss of carrier-mediated transport from the air side of the lung to the blood side was observed (Williams et al., 1980). These changes imply an effect on the barrier function of the lung, which regulates fluxes of various substances with potential physiological activities across the alveolar walls.

The biochemical effects observed in experimental animals exposed to ozone are summarized in Figure 1-12 and Table 1-15 (see Section 1.10.1 for criteria used in developing this summary).

1.10.3.4 _Effects of Ozone in Altering Host Defense Against Microbes_. Reports over the years have presented substantial evidence that exposure to ozone significantly increases the ability of an inhaled infectious microorganism to colonize and to proliferate within the lung, resulting in significant increases in mortality. This response is dose-related and is significant at concentrations of ozone as low as 0.08 to 0.1 ppm (Coffin et al., 1968; Ehrlich et al., 1977; Miller et al., 1978; Aranyi et al., 1983). The biological basis for this response appears to be that ozone or one of its reactive products can impair the normal bactericidal pulmonary defenses, which results in prolonging the life of the infectious agent, permitting its multiplication, and ultimately,

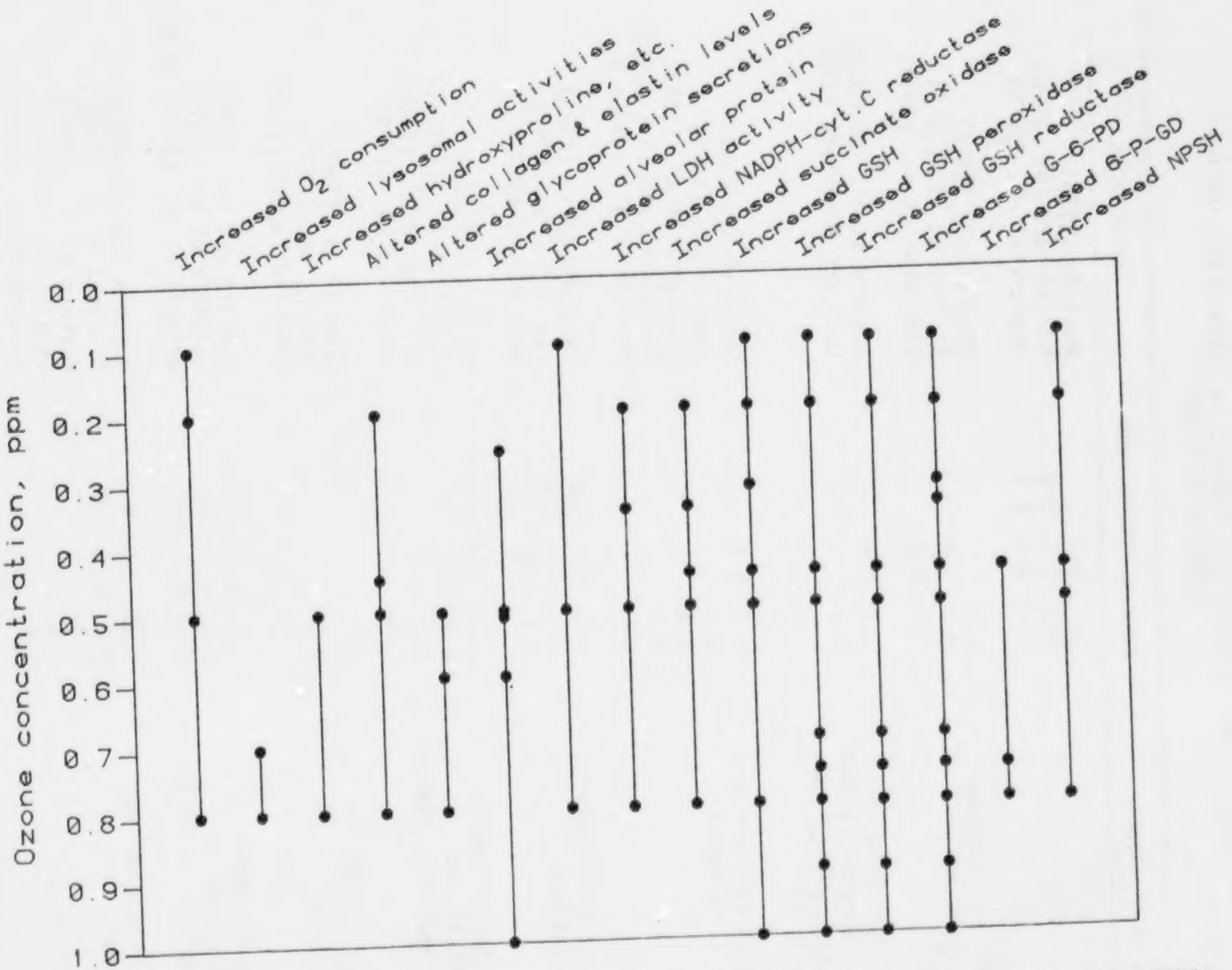

Figure 1-12. Summary of biochemical changes in experimental animals exposed to ozone. See Table 1-15 for reference citations for studies summarized here.

TABLE 1-15. BIOCHEMICAL CHANGES IN EXPERIMENTAL ANIMALS EXPOSED TO OZONE

Effect/response	O_3 concentration, ppm	References
Increased O_2 consumption	0.1, 0.2	Mustafa (1975)
	0.1, 0.2, 0.8	Mustafa and Lee (1976)
	0.2, 0.5, 0.8	Mustafa et al. (1973)
Increased lysosomal activities	0.8	Chow et al. (1974)
	0.7, 0.8	Dillard et al. (1972)
	0.7, 0.8	Castleman et al. (1973)
Increased lung hydroxyproline and prolylhydroxylase activity	0.5, 0.8	Hussain et al. (1976a,b)
	0.5	Last and Greenberg (1980)
Altered collagen and elastin levels	0.2, 0.8	Costa et al. (1983)
	0.5	Last et al. (1979)
	0.45	Bhatnagar et al. (1983)
	0.8	Hesterberg and Last (1981)
	0.8	Hussain et al. (1976a,b)
Altered glycoprotein secretions	0.5, 0.6, 0.8	Last and Kaizu (1980)
	0.5, 0.6, 0.8	Last and Cross (1978)
	0.6, 0.8	Last et al. (1977)
Increased alveolar protein and permeability changes	0.26, 0.51, 1.0	Hu et al. (1982)
	0.5, 1.0	Alpert et al. (1971a)
	0.6, 1.0	Williams et al. (1980)
	1.0	Reasor et al. (1979)
Increased LDH activity	0.1	Chow et al. (1981)
	0.5	Chow et al. (1977)
	0.8	Chow and Tappel (1973)
Increased NADPH - cytochrome -C- reductase activity	0.2, 0.35, 0.8	Mustafa and Lee (1976)
	0.2, 0.5, 0.8	Schwartz et al. (1976)
	0.2, 0.5, 0.8	Delucia et al. (1972, 1975)
Increased succinate oxidase	0.35, 0.5, 0.8	Mustafa and Lee (1976)
	0.2, 0.5, 0.8	Schwartz et al. (1976)
	0.45	Mustafa et al. (1982)
	0.8	Chow et al. (1976)
	0.8	Elsayed et al. (1982a)
Increased GSH	0.1	Chow et al. (1981)
	0.5, 1.0	Fukase et al. (1978)
	0.2, 0.5, 1.0	Fukase et al. (1975)
	0.8	DeLucia et al. (1975)
	0.32	Moore et al. (1980)
	0.45	Mustafa et al. (1982)
	0.5	Chow et al. (1975)

TABLE 1-15. BIOCHEMICAL CHANGES IN EXPERIMENTAL ANIMALS EXPOSED TO OZONE (continued)

Effect/response	O_3 concentration, ppm	References
Increased GSH peroxidase	0.1	Chow et al. (1981)
	0.1, 0.2	Plopper et al. (1979)
	0.2, 0.5, 0.8	Mustafa and Lee (1976)
	0.2, 0.5, 0.8	Chow et al. (1974)
	0.5, 1.0	Fukase et al. (1975)
	0.45	Mustafa et al. (1982)
	0.5	Chow et al. (1975)
	0.7, 0.75	Chow and Tappel (1972, 1973)
	0.8	Chow et al. (1976)
	0.9	Tyson et al. (1982)
Increased GSH reductase	0.9	Tyson et al. (1982)
	0.8	Chow et al. (1976)
	0.1	Chow et al. (1981)
	0.1, 0.2	Plopper et al. (1979)
	0.2, 0.5, 0.8	Mustafa and Lee (1976)
	0.2, 0.5, 0.8	Chow et al. (1974)
	0.5, 1.0	Fukase et al. (1975)
	0.2, 0.5, 0.8	DeLucia et al. (1975)
	0.45	Mustafa et al. (1982)
	0.5	Chow et al. (1975)
	0.7, 0.75	Chow and Tappel (1972, 1973)
Increased G-6-PD	0.9	Lunan et al. (1977)
	0.9	Tyson et al. (1982)
	0.8	Elsayed et al. (1982a)
	0.8	Chow et al. (1976)
	0.7, 0.75	Chow and Tappel (1972, 1973)
	0.1	Chow et al. (1981)
	0.1, 0.2	Plopper et al. (1979)
	0.2, 0.35, 0.5, 0.8	Mustafa and Lee (1976)
	0.5, 0.8	Chow et al. (1974)
	0.2, 0.5, 0.8	Schwartz et al. (1976)
	0.5, 1.0	Fukase et al. (1975)
	0.2, 0.5, 0.8	DeLucia et al. (1972, 1975)
	0.32	Moore et al. (1980)
	0.45	Mustafa et al. (1982)
	0.5	Chow et al. (1975)
Increased 6-P-GD	0.45	Mustafa et al. (1982)
	0.75, 0.8	Chow and Tappel (1973)
	0.8	Elsayed et al. (1982a,b; 1983)
Increased NPSH	0.1, 0.2	Plopper et al. (1979)
	0.2, 0.5, 0.8	DeLucia et al. (1975)
	0.45	Mustafa et al. (1982)
	0.8	Chow et al. (1976)

in this animal model, resulting in death. Such infections occur because of a breakdown in a complex host defense system involving tissue morphology, transport mechanisms, phagocytic ability, and various immune factors.

The data obtained in various experimental animal studies indicate that short-term ozone exposure can reduce the effectiveness of several vital defense systems including (1) the ability of the lung to inactivate bacteria and viruses (Coffin et al., 1968; Coffin and Gardner, 1972a,b; Goldstein et al., 1974, 1977; Hurst et al., 1970; Hurst and Coffin, 1971; Ibrahim et al., 1976; Nakajima et al., 1972; Ehrlich et al., 1979); (2) the mucociliary transport system (Phalen et al., 1980; Frager et al., 1979; Kenoyer et al., 1981; (3) the immunological system (Campbell and Hilsenroth, 1976; Thomas et al., 1981; Aranyi et al., 1983; and (4) the pulmonary macrophage (Dowell et al., 1970; Goldstein et al., 1971; Hadley et al., 1977; McAllen et al., 1981; Witz et al., 1983; Amoruso et al., 1981). Studies have also indicated that the activity level of the test subject and the presence of other airborne chemicals are important variables that can influence the determination of the lowest effective concentration of the pollutant (Gardner et al., 1977; Aranyi et al., 1983; Ehrlich, 1980, 1983; Grose et al., 1980, 1982; Phalen et al., 1980; Goldstein et al., 1974; Illing et al., 1980).

A major problem remains in assessing the relevance of these animal data to humans. If this animal model is to be used to reflect the toxicological response occurring in humans, then the endpoint for comparison of such studies should not be mortality, since today few individuals die of bacterial pneumonias. A better comparison in humans would be the increased prevalence of respiratory illness in the community. Such a comparison is proper since both mortality from respiratory infections (animals) and morbidity from respiratory infections (humans) result from a loss in pulmonary defenses.

Ideally, studies of pulmonary host defenses should be performed in man, using epidemiological or volunteer methods of study. Unfortunately, such studies have not been reported yet. Attention must therefore be paid to the results of host-defense experiments conducted with animals.

In the area of host defense, present knowledge of the physiology, metabolism, and function have come primarily from the study of various animal systems, but it is generally accepted that the basic mechanisms of action of these defense cells and systems function similarly in both animals and man. The effects seen in animals represent alterations in basic biological systems. One would not expect to see an equivalent response (e.g., mortality) in man, but one can assume that similar alterations in basic defense mechanisms could occur in humans since they possess equivalent pulmonary defense systems. It is understood, however, that different exposure levels may be required to produce similar responses in humans. The concentration of ozone at which effects become evident can be influenced by a number of factors, such as preexisting disease, dietary factors, concurrent exposure to other pollutants, or the presence of other environmental stresses, or a combination of these. Thus, one could hypothesize that humans exposed to ozone could experience similar effects. At the present time, however, one cannot predict the exact concentration at which effects may occur in man nor the severity of the effects.

The effects of ozone on host defense mechanisms in experimental animals are summarized in Figure 1-13 and Table 1-16 (see Section 1.10.1 for criteria used in developing this summary).

1.10.3.5 Tolerance. Examination of responses to short-term, repeated exposures to O_3 clearly indicates that with some of the parameters measured, animals have an increased capacity to resist the effects of subsequent exposure. This tolerance persists for varying times, depending on the degree of development of the tolerance. Previous low levels of exposure to O_3 will certainly protect against subsequent lethal doses and the development of edema (Stokinger et al., 1956; Fairchild, 1967; Coffin and Gardner, 1972a). The delay in mucociliary activity (i.e., clearance reported for O_3) can also be eliminated by preexposure to a lower concentration. This effect is only for a short period of time and is lost as soon as the mucus secretion rate returns to normal. However, not all of the toxic effects of O_3, such as reduced functioning activity of the pulmonary defense system (Gardner et al., 1972); hyperplasia of the type 2 cells (Evans et al., 1971, 1976a,b); increased susceptibility to respiratory disease (Gardner and Graham, 1977); loss of pulmonary enzymatic activity (Chow, 1976, Chow et al., 1976); and inflammatory response (Gardner et al., 1972) can be prevented by prior treatment with low levels of O_3. Dungworth et al. (1975b) and Castleman et al. (1980) have attempted to explain tolerance by careful examination of the morphological changes that occur with repeated O_3 exposures. These investigators suggest that during continuous exposure to O_3 the injured cells attempt to initiate early repair of the specific lesion. This repair thus results in a reduction of the effect first observed. At this time, there are a number of hypotheses proposed to explain the mechanism of this phenomenon (Mustafa and Tierney, 1978; Schwartz et al., 1976; Mustafa et al., 1977; Berliner et al., 1978; Gertner et al., 1983b;

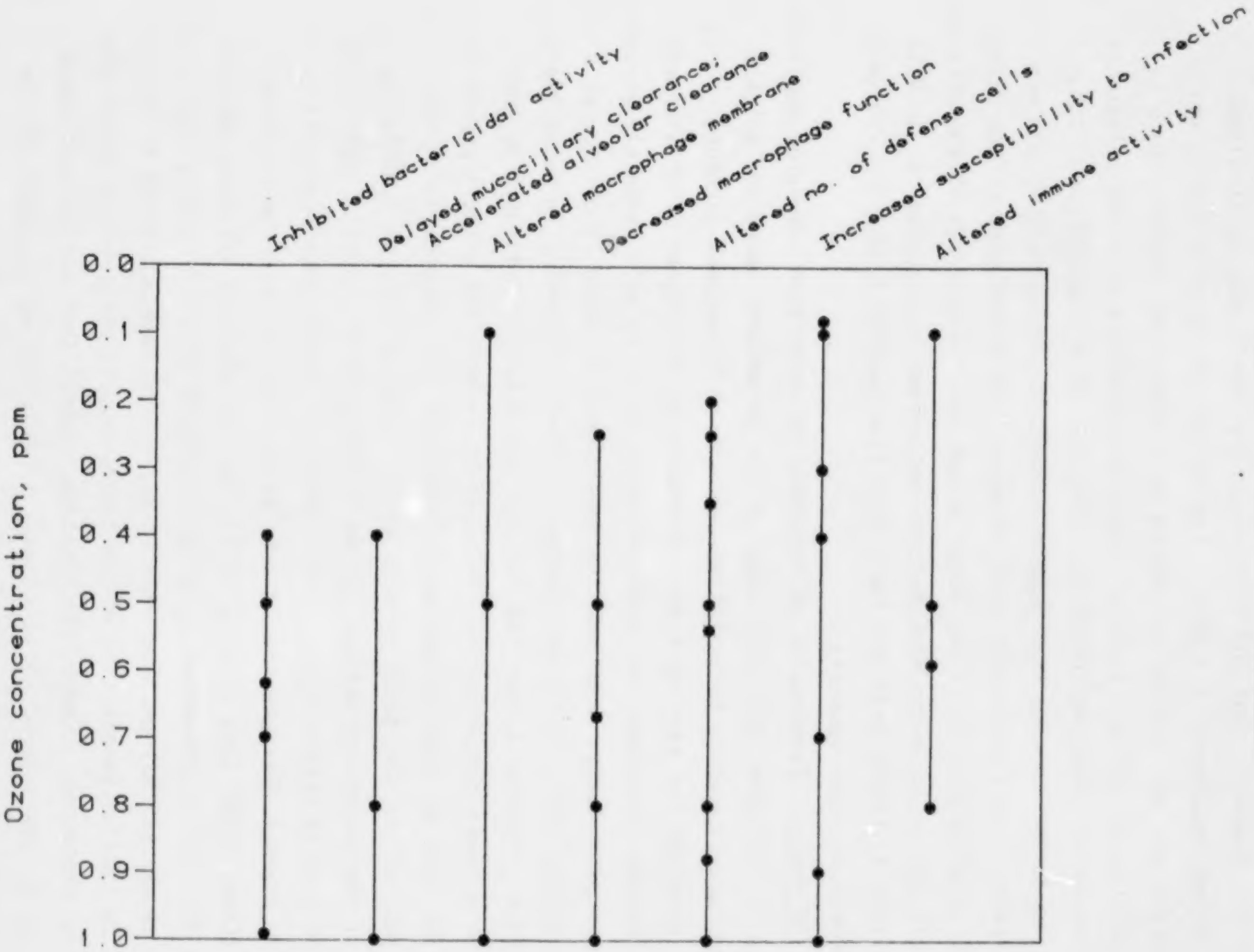

Figure 1-13. Summary of effects of ozone on host defense mechanisms in experimental animals. See Table 1-16 for reference citations for studies summarized here.

TABLE 1-16. EFFECTS OF OZONE ON HOST DEFENSE MECHANISMS IN EXPERIMENTAL ANIMALS

Effect/response	O_3 concentration, ppm	References
Inhibited bactericidal activity	0.5	Friberg et al. (1972)
	0.99	Goldstein et al. (1971a)
	0.62	Goldstein et al. (1971b)
	0.7	Bergers et al. (1983)
	0.7	Warshauer et al. (1974)
	0.4	Coffin and Gardner (1972b)
	0.4	Goldstein, E., et al. (1972)
Delayed mucociliary clearance; accelerated alveolar clearance	0.4, 0.8, 1.0	Kenoyer et al. (1981)
	1.0	Abraham et al. (1980)
	0.8	Phalen et al. (1980)
Altered macrophage membrane	0.1, 1.0	Gardner et al. (1971)
	0.5	Dowell et al. (1970)
	0.5	Hadley et al. (1977)
	0.5, 1.0	Goldstein et al. (1977)
Decreased macrophage function	0.25, 0.5	Hurst et al. (1970, 1971)
	0.5	Alpert et al. (1971b)
	0.5, 0.67	Coffin et al. (1968)
	0.5, 0.67	Coffin and Gardner (1972b)
	0.8	Schwartz and Christman (1979)
	1.0	Shingu et al. (1980)
	1.0	McAllen et al. (1981)
Altered no. of defense cells	0.2	Plopper et al. (1979)
	0.2, 0.35, 0.5, 0.8	Dungworth et al. (1975b)
	0.2, 0.35	Castleman et al. (1977)
	0.2, 0.5, 0.8	Boorman et al. (1977, 1980)
	0.25	Barry et al. (1983)
	0.5	Zitnik et al. (1978)
	0.5, 0.88	Stephens et al. (1974a)
	0.5	Last et al. (1979)
	0.54, 0.88	Freeman et al. (1974)
	0.8	Castleman et al. (1980)
	1.0	Freeman et al. (1973)
	1.0	Cavender et al. (1977)
	0.5, 0.88	Brummer et al. (1977)
	0.5, 0.8	Eustis et al. (1981)
	0.2	Dungworth (1976)
	0.2	Stephens et al. (1976)
Increased susceptibility to infection	0.08	Coffin et al. (1968)
	0.08, 0.1	Miller et al. (1978)
	0.1	Ehrlich et al. (1977)
	0.1	Aranyi et al. (1983)
	0.1, 0.3	Illing et al. (1980)
	0.4, 0.7	Bergers et al. (1983)

TABLE 1-16. EFFECTS OF OZONE ON HOST DEFENSE MECHANISMS IN EXPERIMENTAL ANIMALS (continued)

Effect/response	O_3 concentration, ppm	References
Increased susceptibility (cont'd)	0.3	Abraham et al. (1982)
	0.7, 0.9	Coffin and Blommer (1970)
	1.0	Thomas et al. (1981b)
Altered immune activity	0.1	Aranyi et al. (1983)
	0.5, 0.8	Osebold et al. (1979, 1980)
	0.5, 0.8	Gershwin et al. (1981)
	0.59	Campbell and Hilsenroth (1976)

Bhatnagar et al., 1983). From this literature, it would appear that tolerance, as seen in animals, may not be the result of any one single biological process, but instead may result from a number of different routes, depending on the specific response measured. Tolerance does not imply complete or absolute protection, because continuing injury does still occur, which could potentially lead to nonreversible pulmonary changes.

1.10.4 Extrapulmonary Effects of Ozone

It was formerly believed that O_3, on contact with respiratory system tissue, immediately reacted and thus was not absorbed or transported to extrapulmonary sites. However, several studies suggest that either O_3 or products formed by the interaction of O_3 and respiratory system tissue produce effects in lymphocytes, erythrocytes, and serum, as well as in the parathyroid gland, the myocardium, the liver, and the CNS. Ozone exposure also produces effects on animal behavior that may be caused by pulmonary consequences of O_3, or by nonpulmonary (CNS) mechanisms. The mechanism by which O_3 causes extrapulmonary changes is unknown. Mathematical models of O_3 dosimetry predict that very little O_3 penetrates to the blood of the alveolar capillaries. Whether these effects result from O_3 or a reaction product of O_3 which penetrates to the blood and is transported is the subject of speculation.

1.10.4.1 Central Nervous System and Behavioral Effects. Ozone significantly affects the behavior of rats during exposure to concentrations as low as 235 $\mu g/m^3$ (0.12 ppm) for 6 hr. With increasing concentrations of O_3, further decreases in unspecified motor activity and in operant learned behaviors have been observed (Konigsberg and Bachman, 1970; Tepper et al., 1982; Murphy et al., 1964; and Weiss et al., 1981). Tolerance to the observed decrease in motor activity may occur on repeated exposure. At low O_3 exposure concentrations (490 μg/m^3, 0.25 ppm) an increase in activity is observed after exposure ends. Higher O_3 concentrations (980 μg/m^3, 0.5 ppm) produce a decrease in rodent activity that persists for several hours after the end of exposure (Tepper et al., 1982, 1983).

The mechanism by which behavioral performance is reduced is unknown. Physically active responses appear to enhance the effects of O_3, although this may be the result of an enhanced minute volume that increases the effective concentration delivered to the lung. Several reports indicate that it is unlikely that animals have reduced physiological capacity to respond, prompting Weiss et al. (1981) to suggest that O_3 impairs the inclination to respond. Two studies indicate that mice will respond to remove themselves from an atmosphere containing greater than 980 μg/m^3 (0.5 ppm) (Peterson and Andrews, 1963, Tepper et al., 1983). These studies suggest that the aversive effects of O_3 may be due to lung irritation. It is unknown whether lung irritation, odor, or a direct effect on the CNS causes change in rodent behavior at lower O_3 concentrations.

1.10.4.2 Cardiovascular Effects. Studies on the effects of O_3 on the cardiovascular system are few, and to date there are no reports of attempts to confirm these studies. Structural changes in the cell membranes and nuclei of the myocardium muscle fibers in mice were found after 3 weeks of exposure to 392 μg/m^3 (0.2 ppm) (Brinkman et al., 1964), and these effects were reversible in clean air. The exposure of rats to O_3 alone or in combination with cadmium (1176 μg/m^3, 0.6 ppm O_3) resulted in measurable increases in systolic pressure and heart rate (Revis et al., 1981). No additive or antagonistic response was observed with the combined exposure. Pulmonary capillary blood flow and PaO_2 decreased 30 min following exposure of dogs to 588 μg/m^3 (0.3 ppm) of O_3 (Friedman et al., 1983). The decrease in pulmonary capillary blood flow persisted for as long as 24 hr following exposure.

1.10.4.3 Hematological and Serum Chemistry Effects. The data base for the effects of O_3 on the hematological system is extensive and indicates that O_3 or one of its reactive products can cross the blood-gas barrier, causing changes in the circulating erythrocytes (RBC) as well as significant differences in various components of the serum.

Effects of O_3 on the circulating RBCs can be readily identified by examining either morphological and/or biochemical endpoints. These cells are structually and metabolically well understood and are available through relatively non-invasive methods, which makes them ideal candidates for both human and animal studies. A wide range of structural effects have been reported in a variety of species of animals, including an increase in the fragility of RBCs isolated from monkeys exposed to 1470 $\mu g/m^3$ (0.75 ppm) of O_3 4 hr/day for 4 days (Clark et al., 1978). A single 4-hr exposure to 392 $\mu g/m^3$ (0.2 ppm) also caused increased fragility as well as sphering of RBCs of rabbits (Brinkman et al., 1964). An increase in the number of RBCs with Heinz bodies was detected following a 4-hr exposure to 1666 $\mu g/m^3$ (0.85 ppm). The presence of such inclusion bodies in RBCs is an indication of oxidant stress (Menzel et al., 1975a).

These morphological changes are frequently accompanied by a wide range of biochemical effects. RBCs of monkeys exposed to 1470 $\mu g/m^3$ (0.75 ppm) of O_3 for 4 days also had a decreased level of glutathione (GSH) and decreased acetylcholinesterase (AChE) activity, an enzyme bound to the RBC membranes. The RBC GSH activity remained significantly lower 4 days postexposure (Clark et al., 1978).

Animals deficient in vitamin E are uniquely sensitive to O_3. The RBCs from these animals, after being exposed to O_3, had a significant increase in the activity of GSH peroxidase, pyruvate kinase, and lactic dehydrogenase, but had a decrease in RBC GSH after exposure to 1568 $\mu g/m^3$ (0.8 ppm) for 7 days (Chow and Kaneko, 1979). Animals with a vitamin E-supplemented diet did not have any changes in glucose-6-phosphate dehydrogenase (G-6-PD), superoxide dismutase, or catalase activities. At a lower level (980 $\mu g/m^3$, 0.5 ppm), there were no changes in GSH level or in the activities of GSH peroxidase or GSH reductase (Chow et al., 1975). Menzel et al. (1972) also reported a significant increase in lysis of RBCs from vitamin E-deficient animals after 23 days of exposure to 980 $\mu g/m^3$ (0.5 ppm). These effects were not observed in vitamin E-supplemented rats. Mice on a vitamin E-supplemented diet and those on a deficient diet showed an increase in G-6-PD activity after an exposure of 627 $\mu g/m^3$ (0.32 ppm) of O_3 for 6 hr. Decreases observed in AChE activity occurred in both groups (Moore et al., 1980).

Other blood changes are attributed to O_3. Rabbits exposed for 1 hr to 392 $\mu g/m^3$ (0.2 ppm) of O_3 showed a significant drop in total blood serotonin (Veninga, 1967). Six- and 10-month exposures of rabbits to 784 $\mu g/m^3$ (0.4 ppm) of O_3 produced an increase in serum protein esterase and in serum trypsin inhibitor. This latter effect may be a result of thickening of the small pulmonary arteries. The same exposure caused a significant decrease in albumin levels and an increase in alpha and gamma globulins (P'an and Jegier, 1971, 1976; P'an et al., 1972; and Jegier, 1973). Chow et al. (1974) reported that the serum lysozyme level of rats increased significantly after 3 days of continuous exposure to O_3 but was not affected when the exposure was intermittent (8 hr/day, 7 days). The O_3 concentration in both studies was 1568 $\mu g/m^3$ (0.8 ppm) of O_3.

Short-term exposure to low concentrations of O_3 induced an immediate change in the serum creatine phosphokinase level in mice. In this study, the O_3 doses were expressed as the product of concentration and time. The C x T value for this effect ranged from 0.4 to 4.0 (Veninga et al., 1981).

A few of the hematological effects observed in animals (i.e., decrease in GSH and AChE activity and the formation of Heinz bodies) following exposure to O_3 have also been seen following in vitro exposure of RBCs from humans (Freeman and Mudd, 1981; Menzel et al., 1975b; Verweij and Van Steveninck, 1981). A common effect observed by a number of investigators is that O_3 inhibits the membrane ATPase activity of RBCs (Koontz and Heath, 1979; Kesner et al., 1979; Kindya and Chan, 1976; Freeman et al., 1979; Verweij and Van Steveninck, 1980). It has been postulated that this inhibition of ATPase could be related to the spherocytosis and increased fragility of RBCs seen in animal and human cells.

Although these in vitro data are useful in studying mechanisms of action, it is difficult to extrapolate these data to any effects observed in man. Not only is the method of exposure not physiological, but the actual concentration of O_3 reaching the RBC cannot be determined with any accuracy.

1.10.4.4 Cytogenetic and Teratogenic Effects

Uncertainty still exists regarding possible reproductive, teratogenic, and mutational effects of exposure to ozone. Based on various in vitro data, a number of chromosomal effects of ozone have been described for isolated cultured cell lines, human lymphocytes, and microorganisms (Fetner, 1962; Hamelin et al., 1977a, 1977b, 1978; Hamelin and Chung, 1975, 1978; Scott and Lesher, 1963; Erdman and Hernandez, 1982; Guerrero et al., 1979; Dubean and Chung, 1979, 1982). The interpretation, relevance, and predictive values of such studies to human health are questionable since (1) the concentrations used were many-fold greater than what is found in the ambient air (see

Chapter 10); (2) attempts to extrapolate in vitro exposure concentrations to human exposure dose is not yet possible; and (3) direct exposure of isolated cells to ozone is highly artifactual since it bypasses all the defenses of the host that would normally be functioning in protecting the individual from the inhaled gas. Furthermore, the direct exposure of isolated cells in vitro to ozone may result in chemical reactions between ozone and culture media that might not occur in vivo.

Important questions still exist regarding in vivo cytogenetic effects of ozone in rodents and humans. In 1971, Zelac et al. reported chromosomal abnormalities in peripheral leukocytes of hamsters exposed to O_3 (0.2 ppm). Combined exposures to ozone and radiation (227-233 rads) produced an additive effect on the number of chromosome breaks in peripheral leukocytes. These specific findings were not confirmed by Gooch et al. (1976) or by Tice et al. (1978), but sufficient differences in the various experimental protocols make a direct comparison difficult. The latter group did report significant increases in the number of chromatid deletions and achromatic lesions resulting from exposure to 0.43 ppm ozone.

Because the volume of air inspired during pregnancy is significantly enhanced, the pregnant animal may be at greater risk to low levels of ozone exposure. Early studies on the possible teratogenic effects of ozone have suggested that exposures as low as 0.2 ppm can reduce infant survival rate and cause unlimited incisor growth (Brinkman et al., 1964; Veninga et al., 1967). Kavlock et al. (1979, 1980) found that pregnant rats exposed to 1.0 and 1.49 ppm ozone showed a significant increase in embryo resorption rate, slower growth, slower development of righting reflexes, and delayed grooming and rearing behavior.

1.10.4.5 Other Extrapulmonary Effects. A series of studies was conducted to show that O_3 increases drug-induced sleeping time in a number of species of animals (Gardner et al., 1974; Graham, 1979; Graham et al., 1981, 1982a,b, 1983a,b). At 1960 $\mu g/m^3$ (1.0 ppm), effects were observed after 1, 2, and 3 days of exposure. As the concentration of O_3 was reduced, increasing numbers of daily 3-hr exposures were required to produce a significant effect. At the lowest concentration studied (196 $\mu g/m^3$, 0.1 ppm), the increase was observed at days 15 and 16 of exposure. It appears that this effect is not specific to the strain of mouse or to the three species of animals tested, but it is sex-specific, with females being more susceptible. Recovery was complete within 24 hr after exposure. Although a number of mechanistic studies have been conducted, the reason for this effect on pentobarbital-induced sleeping time is not known. It has been hypothesized that some common aspect related to liver drug metabolism is quantitatively reduced (Graham et al., 1983a).

Several investigators have attempted to elucidate the involvement of the endocrine system in O_3 toxicity. Most of these studies were designed to investigate the hypothesis that the survival rate of mice and rats exposed to lethal concentrations of O_3 could be increased by use of various thyroid blocking agents or by thyroidectomy. To follow up these findings, Clemons and Garcia (1980a,b) investigated the effects of a 24-hr exposure to 1960 $\mu g/m^3$ (1.0 ppm) of O_3 on the hypothalamo-pituitary-thyroid system of rats. These three organs regulate the function of each other through various hormonal feedback mechanisms. Ozone caused decreases in serum concentration of thyroid stimulating hormone (TSH), in circulating thyroid hormones (T_3 and T_4) and in protein-bound iodine. No alterations were observed in many other hormone levels measured. Thyroidectomy prevented the effect of O_3 on TSH. The thyroid gland itself was altered (e.g., edema) by O_3. The authors interpreted these findings as an O_3-induced lowering of the hypothalamic set point for the pituitary-thyroid axis and a simultaneous reduction of the activity of prolactin inhibiting factor in the hypothalamus. The anterior pituitaries had fewer cells but more TSH per cell. These cells also released a greater amount of TSH into the culture medium.

The extrapulmonary effects of ozone in experimental animals are summarized in Figure 1-14 and Table 1-17. Criteria used in developing the summary were presented in Section 1.10.1

1.10.5 Effects of Other Photochemical Oxidants

There have been far too few controlled toxicological studies with the other oxidants to permit any sound scientific evaluation of their contribution to the toxic action of photochemical oxidant mixtures. The few toxicological studies on PAN indicate that it is much less acutely toxic than O_3. When the effects seen after exposure to O_3 and PAN are examined and compared, it is obvious that the test animals must be exposed to concentrations of PAN much greater than those needed with O_3 to produce a similar effect on lethality, behavior modification, morphology, or significant alterations in host pulmonary defense system (Campbell et al., 1967; Dungworth et al., 1969; Thomas et al., 1979, 1981a). The concentrations of PAN required to produce these effects are many times greater than what has been measured in the atmosphere (0.037 ppm).

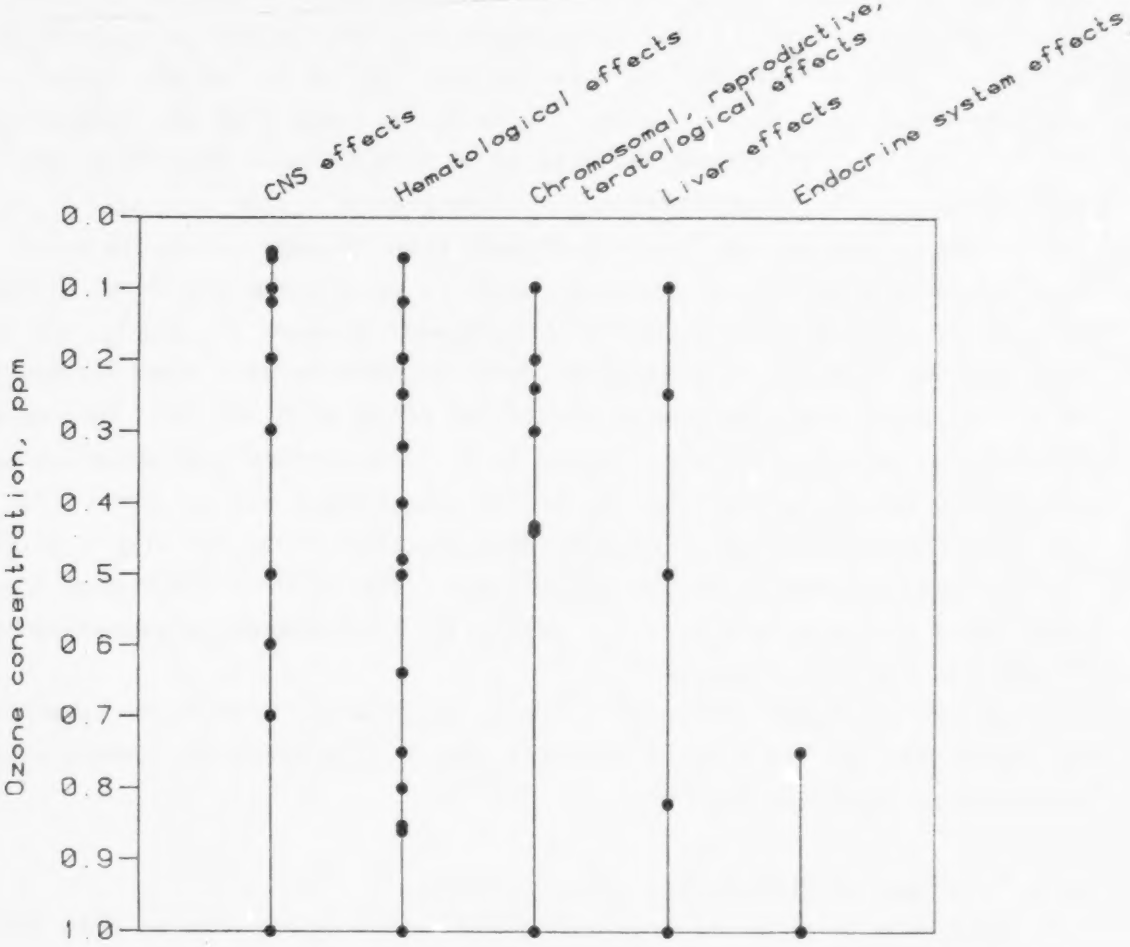

Figure 1-14. Summary of extrapulmonary effects of ozone in experimental animals. See Table 1-17 for reference citations for studies summarized here.

TABLE 1-17. EXTRAPULMONARY EFFECTS OF OZONE IN EXPERIMENTAL ANIMALS

Effect/response	O_3 concentration, ppm	References
CNS effects	0.05, 0.5	Konigsberg and Bachman (1970)
	0.1 - 1.0	Weiss et al. (1981)
	0.12 - 1.0	Tepper et al. (1982)
	0.2, 0.3, 0.5, 0.7	Murphy et al. (1964)
	0.5	Tepper et al. (1983)
	0.5	Reynolds and Chaffee (1970)
	0.5	Xintaras et al. (1966)
	0.6	Peterson and Andrews (1963)
	1.0	Fletcher and Tappel (1973)
	1.0	Trams et al. (1972)
Hematological effects	0.06, 0.12, 0.48	Calabrese et al. (1983a)
	0.2	Brinkman et al. (1964)
	0.2, 1.0	Veninga (1967, 1970) Veninga et al. (1981)
	0.25, 0.32, 0.5	Moore et al. (1980; 1981a,b)
	0.4	Jegier (1973)
	0.4	P'an and Jegier (1972, 1976)
	0.5	Menzel et al. (1972)
	0.64	Larkin et al. (1983)
	0.75	Clark et al. (1978)
	0.8	Chow and Kaneko (1979)
	0.8	Chow et al. (1974)
	0.85	Menzel et al. (1975a)
	0.86	Schlipkoter and Bruch (1973)
	1.0	Dorsey et al. (1983)
	1.0	Mizoguchi et al. (1973)
	1.0	Christiansen and Giese (1954)
Chromosomal, reproductive, teratological effects	0.1	Brinkman et al. (1964)
	0.2	Veninga (1967)
	0.44	Kavlock et al. (1979)
	1.0	Kavlock et al. (1980)
	0.24, 0.3	Zelac et al. (1971a)
	0.43	Tice et al. (1978)
Liver effects	0.1, 0.25, 0.5, 1.0	Graham (1979) Graham et al. (1981, 1982a,b)
	0.82	Veninga et al. (1981)
	1.0	Gardner et al. (1974)
Endocrine system effects	0.75	Atwal and Wilson (1974)
	0.75	Atwal et al. (1975)
	0.75	Atwal and Pemsingh (1981)
	1.0	Clemons and Garcia (1980a,b)

Similarly, most of the investigations reporting H_2O_2 toxicity have involved concentrations much higher than those found in the ambient air (0.1 ppm), or the investigations were conducted by using various in vitro techniques for exposure. Very limited information is available on the health significance of inhalation exposure to gaseous H_2O_2. Because H_2O_2 is highly soluble, it is generally assumed that it does not penetrate into the alveolar regions of the lung but is instead deposited on the surface of the upper airways (Last et al., 1982). Unfortunately, there have not been studies designed to look for possible effects in this region of the respiratory tract.

A few in vitro studies have reported cytotoxic, genotoxic, and biochemical effects of H_2O_2 when using isolated cells or organs (Stewart et al., 1981; Bradley et al., 1979; Bradley and Erickson, 1981; Speit et al., 1982; MacRae and Stich, 1979). Although these studies can provide useful data for studying possible mechanisms of action, it is not yet possible to extrapolate these responses to those that might occur in the mammalian system.

Field and epidemiological studies have shown that human health effects from exposure to ambient mixtures of oxidants and other airborne pollutants can produce adverse human health effects (Chapter 12). Few such studies have been conducted with laboratory animals, because testing and measuring of such mixtures is not only complicated, but extremely costly. In these studies, the investigators attempted to simulate the photochemical reaction products produced under natural conditions and to define the cause-effect relationship.

Exposure to complex mixtures of oxidants plus the various components found in UV-irradiated auto exhaust indicates that certain effects, such as histopathological changes, increase in susceptibility to infection, a variety of altered pulmonary functional activities were observed in this oxidant atmosphere which was not reported in the nonirradiated exhaust (Murphy et al., 1963; Murphy, 1964; Nakajima et al., 1972; Hueter et al., 1966). Certain other biological responses were observed in both treatment groups, including a decrease in spontaneous activity, a decrease in infant survival rate, fertility, and certain pulmonary functional abnormalities (Hueter et al., 1966; Boche and Quilligan, 1960; Lewis et al., 1967).

Dogs exposed to UV-irradiated auto exhaust containing oxidants either with or without SO_x showed significant pulmonary functional abnormalities that had relatively good correlation with structural changes (Hyde et al., 1978; Gillespie, 1980; Lewis et al., 1974). There were no significant differences in the magnitude of the response in these two treatment groups, indicating that oxidant gases and SO_x did not interact in any synergistic or additive manner.

1.11 EFFECTS OF OZONE AND OTHER PHOTOCHEMICAL OXIDANTS IN CONTROLLED EXPOSURES

1.11.1 Pulmonary Function Effects in Controlled Human Studies: Mechanical Function of the Lung

Controlled human exposure (clinical) studies typically evaluate much smaller numbers of subjects for shorter periods of time compared with large-scale population studies. A major advantage of these studies is that exposures to either single pollutants or combinations of pollutants are usually carried out in environmentally controlled chambers in which relative humidity, temperature, and pollutant concentrations are well defined and carefully controlled. Exposure conditions are designed to approximate representative ambient air exposure conditions, especially those thought to be associated with the induction of acute effects. Inherent in the design, however, of controlled human exposure studies are limitations on the range of pollutant exposures, types of subjects studied, and types of effects studied. Conditions are strictly monitored by human rights and medical ethics committees to assure that the experimental exposures to the pollutants being tested will not lead to serious morbidity or irreversible illness. Consequently, the types of acute pulmonary responses assessed in controlled exposure studies could be considered as "transient" and "reversible." Depending, however, upon the population at risk, the method of exposure, and the level of subject activity, the so-called mild and reversible health effects measured in controlled human exposure studies may be indicators of other more serious health effects likely to occur if prolonged or repeated ambient exposures to the same concentrations of pollutants were encountered by study subjects. In addition, relatively small changes in lung function of no particular concern for healthy, non-sensitive adults may be medically important for sensitive individuals or for those having compromised pulmonary functions.

1.11.1.1 General Population. A number of controlled human studies have reported significant decrements in pulmonary function associated with ozone exposure, including the presence of respiratory symptoms. The increased severity of reported symptoms generally parallels the observed impairment in pulmonary function. Table 1-18 summarizes pertinent studies on controlled human exposure to ozone.

TABLE 1-18. SUMMARY TABLE: RESULTS OF CONTROLLED HUMAN EXPOSURES TO OZONE

Ozone[a] concentration µg/m³	Ozone[a] concentration ppm	Measurement[b,c] method	Exposure duration	Activity[d] level (V_E)	Observed effect(s)	No. and sex of subjects	Reference
HEALTHY ADULT SUBJECTS AT REST							
627 1960	0.32 1.0	MAST, NBKI	2 hr	R	Specific airway resistance increased with acetylcholine challenge; subjective symptoms in 3/14 at 0.32 ppm and 8/14 at 1.0 ppm.	13 male 1 female	König et al., 1980
980	0.5	CHEM, NBKI	2 hr	R (10)	Decrement in forced expiratory volume and flow.	40 male (divided into four exposure groups)	Folinsbee et al., 1978
980 1470	0.50 0.75	CHEM, NBKI	2 hr	R (8)	Decrement in forced expiratory volume and flow.	8 male 7 female	Horvath et al., 1979
EXERCISING HEALTHY ADULTS							
235 353 470 588 784	0.12 0.18 0.24 0.30 0.40	CHEM, UV	2.5 hr	IE (65) @ 15-min intervals	Decrement in forced expiratory volume and flow suggested at 0.12 ppm with larger decrements at ≥ 0.18 ppm; respiratory frequency and specific airway resistance increased and tidal volume decreased at ≥ 0.24 ppm; coughing reported at all concentrations, pain and shortness of breath at ≥ 0.24 ppm.	135 male (divided into six exposure groups)	McDonnell et al., 1983
392 686	0.20 0.35	UV, UV	1 hr (mouthpiece)	IE (77.5) @ variable competitive intervals CE (77.5)	Decrement in forced expiratory volume and flow with IE and CE; subjective symptoms increased with O_3 concentration and may limit performance; respiratory frequency increased and tidal volume decreased with CE.	10 male (distance runners)	Adams and Schelegle, 1983

TABLE 1-18 (cont'd). SUMMARY TABLE: RESULTS OF CONTROLLED HUMAN EXPOSURES TO OZONE

Ozone[a] concentration μg/m³	Ozone[a] concentration ppm	Measurement[b,c] method	Exposure duration	Activity[d] level ($\dot{V}_E$)	Observed effect(s)	No. and sex of subjects	Reference
392 823 980	0.2 0.42 0.50	UV, UV	2 hr	IE (30 for male, 18 for female subjects) @ 15-min intervals	Repeated daily exposure to 0.2 ppm did not affect response at higher exposure concentrations (0.42 or 0.50 ppm); large inter-subject variability but individual pulmonary function responses were highly reproducible.	8 male 13 female	Gliner et al., 1983
412	0.21	UV, UV	1 hr	CE (81)	Decrement in forced expiratory volume and flow; subjective symptoms may limit performance.	6 male 1 female (distance cyclists)	Folinsbee et al., 1984
588 980	0.3 0.5	CHEM, NBKI	2 hr	R (10), IE (31, 50, 67) @ 15-min intervals	Decrement in forced expiratory volume and flow; the magnitude of the change was related to O_3 concentration and $\dot{V}_E$. Total lung capacity and inspiratory capacity decreased with IE (50, 67); no change in airway resistance or residual volume even at highest IE (67). No significant changes in pulmonary function were observed at 0.1 ppm.	40 male (divided into four exposure groups)	Folinsbee et al., 1978
725 980 1470	0.37 0.50 0.75	MAST, NBKI	2 hr	R (11) & IE (29) @ 15-min intervals	Good correlation between dose (concentration x $\dot{V}_E$) and decrement in forced expiratory volume and flow.	20 male 8 female (divided into six exposure groups)	Silverman et al., 1976
784	0.4	UV, NBKI	2 hr	IE (2xR) @ 15-min intervals	Specific airway resistance increased with histamine challenge; no changes were observed at concentrations of 0.2 ppm.	12 male 7 female (divided into three exposure groups)	Dimeo et al., 1981
784	0.4	CHEM, NBKI & MAST, UV	3 hr	IE (4-5xR) for 15 min	Decrement in forced expiratory volume was greatest on the 2nd of 5 exposure days; attenuated response by the 4th day of exposure.	10 male 4 female	Farrell et al., 1979

TABLE 1-18 (cont'd). SUMMARY TABLE: RESULTS OF CONTROLLED HUMAN EXPOSURES TO OZONE

Ozone[a] concentration µg/m³	Ozone[a] concentration ppm	Measurement[b,c] method	Exposure duration	Activity[d] level (V_E)	Observed effect(s)	No. and sex of subjects	Reference
784	0.4	CHEM, UV	3 hr	IE (4-5xR) for 15 min	Decrement in forced expiratory volume was greatest on the 2nd of 5 exposure days; attenuation of response occurred by the 5th day and persisted for 4 to 7 days. Enhanced bronchial reactivity with methacholine on the first 3 days; attenuation of response occurred by the 4th and 5th day and persisted for > 7 days.	13 male 11 female (divided into two exposure groups)	Kulle et al., 1982
823	0.42	UV, UV	2 hr	IE (30)	Decrement in forced expiratory volume and flow greatest on the 2nd of 5 exposure days; attenuation of response occurred by the 5th day and persisted for < 14 days with considerable intersubject variability.	24 male	Horvath et al., 1981
921	0.47	UV, NBKI	2 hr	IE (3xR)	Decrement in forced expiratory volume and flow greatest on the 2nd of 4 exposure days; attenuation of response occurred by the 4th day and persisted for 4 days.	8 male 3 female	Linn et al., 1982b
1176	0.6	UV, NBKI	2 hr (noseclip)	IE (2xR) @ 15-min intervals	Specific airway resistance increased in 7 nonatopic subjects with histamine and methacholine and in 9 atopic subjects with histamine.	11 male 5 female (divided by history of atopy)	Holtzman et al., 1979
1470	0.75	MAST, NBKI	2 hr	IE (2xR) @ 15-min intervals	Decrements in spirometric variables (20%-55%); residual volume and closing capacity increased.	12 male	Hazucha et al., 1973

TABLE 1-18 (cont'd). SUMMARY TABLE: RESULTS OF CONTROLLED HUMAN EXPOSURES TO OZONE

Ozone[a] concentration µg/m³	Ozone[a] concentration ppm	Measurement[b,c] method	Exposure duration	Activity[d] level (V_E)	Observed effect(s)	No. and sex of subjects	Reference
ASTHMATICS							
392	0.2	CHEM, NBKI	2 hr	IE (2xR) @ 15-min intervals	No significant changes in pulmonary function. Small changes in blood biochemistry. Increase in symptom frequency reported.	20 male 2 female	Linn et al., 1978
490	0.25	CHEM, NBKI	2 hr	R	No significant changes in pulmonary function.	5 male 12 female	Silverman, 1979
SUBJECTS WITH CHRONIC OBSTRUCTIVE LUNG DISEASE							
235	0.12	UV, NBKI	1 hr	IE (variable) @ 15-min intervals	No significant changes in forced expiratory performance or symptoms. Decreased arterial oxygen saturation during exercise was observed.	18 male 7 female	Linn et al., 1982a
353 490	0.18 0.25	UV, NBKI	1 hr	IE (variable) @ 15-min intervals	No significant changes in forced expiratory performance or symptoms. Group mean arterial oxygen saturation was not altered by O_3 exposure.	15 male 13 female	Linn et al., 1983
392 588	0.2 0.3	CHEM, NBKI	2 hr	IE (28) for 7.5 min each half hour	No significant changes in pulmonary function or symptoms. Decreased arterial oxygen saturation during exposure to 0.2 ppm.	13 male	Solic et al., 1982 Kehrl et al., 1983
784	0.41	UV, UV	3 hr	IE (4-5xR) for 15 min	Small significant decreases in FVC and $FEV_{3.0}$.	17 male 3 female	Kulle et al., 1984

[a] Ranked by lowest observed effect level.

[b] Measurement method: MAST = KI-Coulometric (Mast meter); CHEM = gas phase chemiluminescence; UV = ultraviolet photometry.

[c] Calibration method: NBKI = neutral buffered potassium iodide; UV = ultraviolet photometry.

[d] Minute ventilation reported in L/min or as a multiple of resting ventilation. R = rest; IE = intermittent exercise; CE = continuous exercise.

Studies employing at-rest (no exercise) exposures to ozone have shown that ozone concentrations $\geq$ 0.5 ppm produce significant decrements in pulmonary function. Subsequent studies have employed various levels of exercise will enhance to modify the change in function during ozone exposure. The severity of exercise is expressed in terms of minute ventilation ($\dot{V}_E$). (See Volumes IV and V for a glossary of terms.) Increased minute ventilation accompanying exercise will enhance pulmonary decrements during ozone exposure. While the most recent reports include actual measurements of minute ventilation obtained during exposure, earlier publications often included only a description of the exercise regimen. Table 1-19 presents estimates of the minute ventilation associated with given exercise regimens. This table compares the level of exercise with the work performed (watts or kg-m/min), the minute ventilation required, and representative activities of individuals for that level of work (exercise).

Based on reported studies of 1 to 3 hr duration, significant pulmonary function impairment (decrement) occurs when exercise is combined with exposure to ozone:

1. Light exercise ($\dot{V}_E \leq$ 25 L/min) - Effects at $\geq$ 0.37 ppm O_3;
2. Moderate exercise ($\dot{V}_E$ = 26-43 L/min) - Effects at $\geq$ 0.30 ppm O_3;
3. Heavy exercise ($\dot{V}_E$ = 44-63 L/min) - Effects at $\geq$ 0.24 ppm O_3; and
4. Very heavy exercise ($\dot{V}_E \geq$ 64 L/min) - Effects at $\geq$ 0.18 ppm O_3, with suggestions of decrements at 0.12 ppm O_3.

For the majority of these studies, 15-min intermittent exercise alternated with 15-min rest was employed for the duration of the exposure. Whether the exercise is intermittent or continuous does not appear to affect the pulmonary function response at a given concentration and ventilation.

Experimental design factors that influence the level of pulmonary function changes observed, in terms of group means associated with an exposure study, include the number of subjects tested, timing of the pulmonary function measurements, and the ozone measurement and calibration techniques. A critical minimum number of subjects is required to determine the significance of pulmonary function changes associated with a given ozone exposure. For example, individual responses in males versus females have been difficult to analyze because of the limited number of females in the reported studies. In virtually all of the reported studies, pulmonary function measurements have been made at the

TABLE 1-19. ESTIMATED VALUES OF OXYGEN CONSUMPTION AND MINUTE VENTILATION ASSOCIATED WITH REPRESENTATIVE TYPES OF EXERCISE[a]

Level of work	Work performed watts	Work performed kg-m/min[b]	O_2 consumption, L/min	Minute ventilation, L/min	Representative activities[c]
Light	25	150	0.65	13	Level walking at 2 mph; washing clothes
Light	50	300	0.96	19	Level walking at 3 mph; bowling; scrubbing floors
Light	75	450	1.25	25	Dancing; pushing wheelbarrow with 15-kg load; simple construction; stacking firewood
Moderate	100	600	1.54	30	Easy cycling; pushing wheelbarrow with 75-kg load; using sledgehammer
Moderate	125	750	1.83	35	Climbing stairs; playing tennis; digging with spade
Moderate	150	900	2.12	40	Cycling at 13 mph; walking on snow; digging trenches
Heavy	175	1050	2.47	55	Cross-country skiing; rock climbing; stair climbing with load; playing squash and handball; chopping with axe
Heavy	200	1200	2.83	63	
Very heavy	225	1350	3.19	72	
Very heavy	250	1500	3.55	85	Level running at 10 mph; competitive cycling
Severe	300	1800	4.27	100+	Competitive long distance running; cross-country skiing

[a] See text for discussion.

[b] kg-m/min = work performed each minute to move a mass of 1 kg through a vertical distance of 1 m against the force of gravity.

[c] Adapted from Åstrand and Rodahl (1977).

beginning and end of exposure. Intermittent exercise protocols during exposures would permit pulmonary function to be measured shortly after the completion of each exercise period (during the intervening rest period), but few investigators have included them in their design protocol. The precise timing of this measurement, however, does not appear to be as critical for ozone exposures as it is for sulfur dioxide exposures.

Other variables have not been adequately addressed in the available clinical studies. Information derived from the exposure of smokers and nonsmokers to ozone is sparse and somewhat inconsistent, perhaps partly because of undocumented variability in smoking histories. Although some degree of attenuation appears to occur in smokers, a definite conclusion is not yet possible. Further and more precise studies are required to answer the complex problems associated with personal and ambient pollutant exposures. While a few studies have investigated sex differences in responses to ozone, they have not conclusively demonstrated that men and women respond differently to ozone. Furthermore, gender differences in pulmonary capacities have not been adequately considered in the response evaluation. Environmental conditions such as heat and relative humidity may enhance subjective symptoms and physiological impairment following ozone exposure, but the results to date indicate that the effects are no more than additive. Other variables, such as seasonal effects and age, need to be considered. In particular, responses in the very young and the aged need to be examined. In addition, there may be interactions between and among these variables that may modify the response to O_3, but such information is generally lacking.

In the majority of the studies reported, assessment of the significance of results was typically based on the mean ± variance of changes in lung function resulting from exposure to ozone as compared to exposure to control clean air. Decrements in pulmonary function can be expressed as a function of the effective dose of ozone, where effective dose is defined as the product of ozone concentration, minute ventilation, and exposure duration. The relative contribution of these variables to pulmonary decrements is greater for ozone concentration than for minute ventilation, which is greater than that for exposure duration. Figure 1-15 uses the pulmonary function measurement FEV_1 for relating group mean decrements in lung function to ozone concentration and ventilation. Other measures of spirometric pulmonary function (volumes and flows) are consistent with FEV_1 and hence are not depicted here. Although mean changes are useful for making statistical inferences about homogeneous

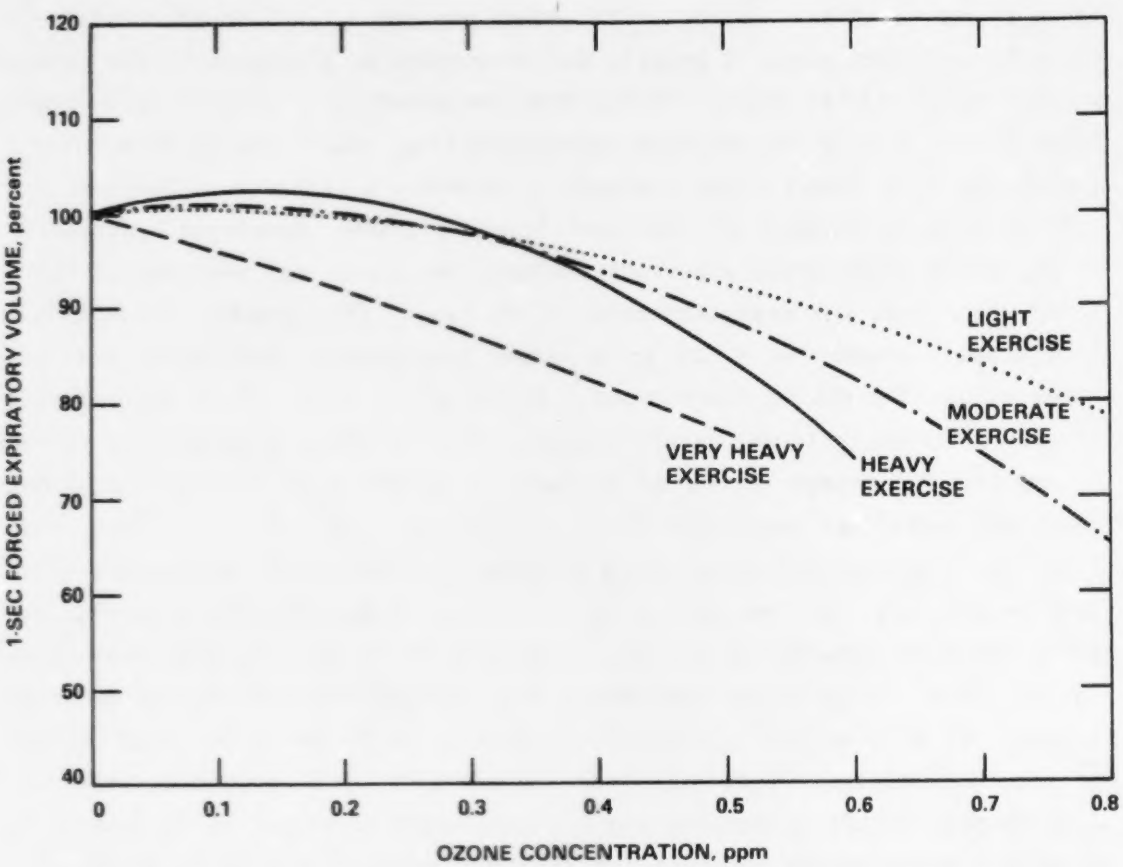

Figure 1-15. Group mean decrements in 1-sec forced expiratory volume during 2-hr ozone exposures with different levels of intermittent exercise: light ($\dot{V}_E \leq 25$ L/min); moderate ($\dot{V}_E$ = 26-43 L/min); heavy ($\dot{V}_E$ = 44-63 L/min); and very heavy ($\dot{V}_E \geq 64$ L/min). (Concentration-response curves are taken from Figures 13-2 to 13-5 in Chapter 13, Volume V).

populations, they may not be adequate for describing differences in responsiveness to ozone among individuals. While the significant mean changes observed demonstrate that the differences in response between ozone and clean air exposures are not the result of chance, the variance of responses was quite large in many studies. Characterization of reports of individual responses to ozone is pertinent since it permits the assessment of a segment of the general population or special subpopulations that are potentially at-risk to O_3 exposure. Since there is good intrasubject reproducibility, the response of a given individual to a single ozone exposure is probably a reliable estimate of the intrinsic responsiveness of that individual to ozone. Sensitive individuals in any given study group apparently weight the group mean response of that study, such that the mean decrement is the result of a greater contribution from a small proportion of the group rather than more or less equal contributions across the entire study group. In any given study, it is desirable to have a sufficiently large overall subject group in order to be able to perform either post hoc categorization of subjects or determine a distribution of both group and individual responses.

1.11.1.2 Subjects with Preexisting Disease. In the past, individuals with compromised lung function have been considered to be potentially at-risk to ozone exposure compared to healthy nonsmokers (U.S. Environmental Protection Agency, 1978). Significant decrements in pulmonary function are not observed, however, in mild asthmatic subjects exposed to ≤ 0.25 ppm O_3 for 2 hr at rest or with intermittent light exercise. In patients with chronic obstructive lung disease (COLD) performing light intermittent exercise, no decrements in pulmonary function are observed for 1- and 2-hr exposures to ≤ 0.30 ppm O_3. Although these results which are derived from spirometric tests suggest that asthmatics and patients with COLD may not be more sensitive to ozone than are healthy subjects, experimental-design considerations in reported studies suggest that this issue is still unresolved. Ethical concern with triggering adverse reactions in these individuals dictates that experimental protocols use only low ozone concentrations and light-to-moderate exercise levels. In one study, however, subjects with mild chronic bronchitis were exposed to 0.4 ppm ozone and were found to be less sensitive than healthy nonsmokers.

In addition to overt changes in pulmonary function, enhanced nonspecific bronchial reactivity has been observed following exposures to ozone concentrations ≥ 0.3 ppm. Exposure to 0.2 ppm of ozone with intermittent light exercise does not affect nonspecific bronchial reactivity.

1.11.1.3 Intersubject Variability. Group mean decrements in pulmonary function can be predicted with some degree of accuracy when expressed as a function of effective dose of ozone, defined, again, as the product of ozone concentration, minute ventilation, and exposure duration. The relative contribution of these variables to pulmonary decrements, as noted in section 1.11.1.1, is greatest for ozone concentration, followed by minute ventilation and exposure duration, in order. A greater degree of predictive accuracy is obtained if the contribution of each of these variables is appropriately weighted. Several additional factors, however, make the interpretation of prediction equations more difficult. Intrasubject variability is relatively small, and the responses of a given individual to a given ozone concentration are quite reproducible. There is considerable intersubject variability, however, in the magnitude of pulmonary function changes with ozone exposure. The data clearly indicate that some individuals in the general population are more responsive than others to ozone. No information is available to account for these differences. Considering the great variability among individuals in their pulmonary responses to ozone exposure, prediction equations that use some form of effective dose may not be adequate for predicting differences in responsiveness to O_3 among individuals.

1.11.1.4 Attenuation with Repeated Exposures. During repeated daily exposures to ozone, decrements in pulmonary function (spirometric variables) are greatest on the second exposure day; thereafter, pulmonary responsiveness to ozone is attenuated, with smaller decrements occurring on each successive day until the fourth or fifth exposure day, when very small or even no changes are observed. Following a sequence of repeated daily exposures, there is a gradual time-related return of susceptibility of pulmonary function to ozone exposure similar to that observed prior to repeated exposures. This attenuated pulmonary responsiveness usually persists for 3 to 7 days, but apparently can last up to 3 weeks in sensitive individuals.

The following general observations appear appropriate: (1) the time required to abolish pulmonary response to ozone is directly related to the magnitude of the initial response; (2) the longer the period required for attenuation of pulmonary response to ozone, the longer the attenuation persists; and (3) the severity of symptomatic responses is associated with the magnitude of functional changes during repeated exposures.

Attenuation of bronchial reactivity has also been observed in response to ozone. The time for attenuation of the initial enhancement in bronchial reactivity is reported to be equivalent to that for decrement in pulmonary function; however, this attenuation appears to last longer.

In studies exposing healthy nonsmokers and subjects with chronic bronchitis to 0.4 ppm ozone, those with chronic bronchitis were less sensitive to ozone, showed attenuation of the initial pulmonary function response earlier, and lost the attenuated response sooner than the healthy nonsmokers.

Repeated daily exposure to a given low (0.20 ppm) concentration of ozone does not affect the magnitude of decrement in pulmonary function resulting from exposure at higher (0.40 to 0.50 ppm) ozone concentrations. This finding is consistent with the proposition that functional adaptation may not occur in the airways of individuals living in communities where the ambient ozone levels do not exceed 0.2 ppm. The difficulty, however, of drawing such inferences on the basis of narrowly defined laboratory studies is that under ambient conditions a number of uncontrollable factors will modify the response. Most notably, other pollutants may interact with ozone to modify changes in the host at lower concentrations during generally more protracted exposures. The evidence suggesting that Los Angeles residents exhibit functional adaptation is sparse and requires confirmation.

Some evidence suggests that exercise performance may be limited by exposure to ozone. Decrements in forced expiratory flow occurring with ozone exposure during prolonged heavy exercise ($\dot{V}_E$ = 65 to 81 L/min) along with increased respiratory frequency and decreased tidal volume might be expected to produce ventilatory limitations at near maximal exercise. Results from exposure to ozone during high exercise levels (68 to 75 percent of max $\dot{V}O_2$) indicate that discomfort associated with maximal ventilation may be an important factor in limiting performance. There are not enough data available, however, to address this issue adequately.

An issue that merits attention and needs resolution is whether attenuated pulmonary responsiveness is beneficial or detrimental. It may possibly reflect the presence or development of underlying changes in neural responses that are protective and do not exact a physical penalty or it may reflect progressive injury to lung tissues.

1.11.2 Other Effects of Ozone in Controlled Human Exposures

No consistent cytogenetic or functional changes have been demonstrated in circulating lymphocytes from human subjects exposed to ozone concentrations as high as 0.4 to 0.6 ppm. Chromosome or chromatid aberrations would therefore be unlikely at lower ozone levels. Limited data have indicated that ozone can interfere with biochemical mechanisms in blood erythrocytes and sera, but the physiological significance of these studies is questionable.

1.11.3 Effects of Peroxyacetyl Nitrate and Mixtures in Controlled Human Exposures

No significant enhancement of respiratory effects has been consistently demonstrated for combined exposures of ozone with sulfur dioxide, nitrogen dioxide, and sulfuric acid or particulate aerosols, or with multiple combinations of these pollutants. Most of the available studies with other photochemical oxidants have been limited to a series of studies on the effects of peroxyacetyl nitrate (PAN) on healthy young and middle-aged males during intermittent exercise on a treadmill. No significant effects were observed at PAN concentrations of 0.25 to 0.27 ppm, which are an order of magnitude higher than the daily maximum concentrations of PAN reported for relatively high oxidant areas of the country (0.047 ppm). Two additional studies at 0.24 and 0.30 ppm of PAN have suggested a possible limitation on forced expiratory volume and flow, but there are not enough data yet for evaluating the significance of this effect. Further studies are also required on the more complex mixtures of pollutants found in the natural environment.

1.12 FIELD AND EPIDEMIOLOGICAL STUDIES OF THE EFFECTS OF OZONE AND OXIDANTS

1.12.1 Introduction

Field and epidemiological studies, when properly executed, offer a unique view of health effects research because they involve the real world, i.e., the study of human populations in their natural setting. However, these studies also have attendant limitations that must be considered in a critical evaluation of their results. One major problem in singling out the effects of one pollutant in field studies of either morbidity or mortality in populations has been the interference of other critical variables in the environment. Limitations also exist for epidemiological research on the health effects of oxidants, including interference or interaction between oxidants and other pollutants; meteorological factors such as temperature; proper exposure assessments including individual activity patterns and location of pollutant monitors; difficulty in identifying oxidant species responsible for observed effects; and characteristics of the populations such as hygiene practices, smoking habits, and socioeconomic status.

Investigative approaches comparing communities with high O_3 concentrations to those with low O_3 concentrations have usually been unsuccessful, often because actual pollutant levels have not differed enough during the study and other important variables have not been adequately controlled. The terms "oxidant" and "ozone" and their association with health effects are often insufficiently clarified. Moreover, our knowledge about the measurement and calibration methods used is still lacking. Also, as our knowledge and skills in epidemiology improve, the incorporation of new key variables into the analyses is required. Thus, the incorporation of individual exposure data (e.g., from the home and workplace) becomes more of a necessity.

Both acute and chronic exposure situations have been reported in the literature on photochemical oxidants. Relevant studies providing quantitative information on effects associated with acute exposure include those on irritative symptoms, pulmonary function, and aggravation of existing respiratory disease (Table 1-20). A few studies, of limited quality, have been reported on morbidity, mortality, and chromosomal effects from chronic exposures.

1.12.2 Field and Epidemiological Studies of Effects of Acute Exposure

Studies on the irritative effects of O_3 have been complicated by the presence of other photochemical oxidants and their precursors in the ambient environment. That O_3 causes the eye irritation normally associated with smog is doubtful. Nevertheless, studies indicate that eye irritation is likely to occur at oxidant levels of about 0.10 ppm. A shown in Table 1-20, associations between oxidant levels and symptoms such as eye, nose, and throat irritation, chest discomfort, cough, and headache have been reported at >0.10 ppm in both children and young adults (Hammer et al., 1974; Makino and Mizoguchi, 1975; Okawada et al., 1979). Zagraniski et al. (1979) also reported an association of these symptoms with approximately 157 $\mu g/m^3$ (0.08 ppm) ozone in adults with asthma and allergies. Discomfort caused by irritative symptoms may be responsible for the impairment of athletic performance reported in high school students during cross-country track meets in Los Angeles (Wayne et al., 1967; Herman, 1972). Although several additional studies have shown respiratory irritation apparently related to ambient exposure in community populations, none of these studies provide satisfactory quantitative data on acute respiratory illnesses.

TABLE 1-20. SUMMARY TABLE: ACUTE EFFECTS OF OZONE AND OTHER PHOTOCHEMICAL OXIDANTS IN POPULATION STUDIES[a]

Lowest estimated effect level, ppm	Average maximum hourly concentration range during study, ppm	Observed effect(s)	Subjects	Reference
OXIDANTS				
b	0.03-0.15	Daily asthma attack rates increased on days with high oxidant and particulate levels and on cool days during a 34-week period in Los Angeles.	Juvenile and adult asthmatics	Whittemore and Korn, 1980
0.10	0.02-0.21	Eye irritation incidence rates increased with oxidant concentration.	Adolescents	Okawada et al., 1979
0.10[c]	<0.23	Symptoms of eye irritation, sore throat, headache, and cough related to oxidant concentration and temperature but not SO_2, NO_2, or NO.	Children and adolescents	Makino and Mizoguchi, 1975
0.10-0.15[c]	<0.04-0.50	Symptoms of eye irritation, cough, chest discomfort, and headache related to oxidant concentration but not carbon monoxide, nitrogen dioxide, or daily minimum temperature.	Young adults	Hammer et al., 1974
0.12[d]	0.06-0.37	Impaired athletic performance related to oxidant concentration but not nitrogen oxide, carbon monoxide, or particulate levels 1 hr before cross-country track meets in Los Angeles.	Adolescents	Wayne et al., 1967 Herman, 1972

TABLE 1-20. SUMMARY TABLE: ACUTE EFFECTS OF OZONE AND OTHER PHOTOCHEMICAL OXIDANTS IN POPULATION STUDIES[a] (continued)

Lowest estimated effect level, ppm	Average maximum hourly concentration range during study, ppm	Observed effect(s)	Subjects	Reference
OZONE				
0.08	0.004-0.235	Increased daily prevalence rates for cough, eye, and nose irritation in smokers and patients with predisposing illnesses; pH of particulate was associated with eye, nose, and throat irritation while suspended sulfates were not associated with any symptoms.	Asthma and allergy patients; normal adults	Zagraniski et al., 1979
0.08	0.01-0.12	Daily peak flows decreased 12.2 to 14.8% with ozone and total suspended particulate matter.	Children and young adults	Lebowitz et al., 1982a, 1983 Lebowitz, 1984
0.08	0.01-0.12	Decreased daily peak flows and increased prevalence rate for acute symptoms associated with ozone, low temperature, and high total suspended particulate matter.	Adult asthmatics	Lebowitz et al., 1982a, 1983 Lebowitz, 1984
0.15	0.01-0.30	Increased airway resistance associated with ozone, sulfur dioxide, and temperature.	Adolescents	Kagawa and Toyoma, 1975 Kagawa et al., 1976; Kagawa, 1983
0.16[e]	0.16-0.17	Small decrement in forced expiratory function and increased symptoms with exercise in both normals and asthmatics.	Normal and asthmatic adults	Linn et al., 1980, 1983

[a] Ranked by lowest estimated effect level for oxidant or ozone.

[b] Not determined.

[c] U.S. Environmental Protection Agency, 1978.

[d] Hasselblad et al., 1976.

[e] Daily mean concentration of ozone was monitored by ultraviolet photometry inside a mobile laboratory; Linn et al., 1980, report concentrations multiplied by 1.25 that correspond to the neutral buffered potassium iodide (KI) method.

Acute epidemiological studies in children and young adults have suggested that decreased peak flow and increased airway resistance occur over the range of O_3 concentrations from 157 to 294 $\mu g/m^3$ (0.08 to 0.15 ppm) (Kagawa and Toyoma, 1975; Kagawa et al., 1976; Kagawa, 1983; Lebowitz et al., 1982a, 1983; Lebowitz, 1984). Qualitative studies support this finding (McMillan et al., 1969; Lebowitz et al., 1974; Fabbri et al., 1979). No controlled human exposure studies in children are presently available for comparison, although studies in adults appear to show no effect below 235 $\mu g/m^3$ (0.12 ppm) O_3 (Chapter 11).

In studies of exacerbation of asthma and chronic lung diseases, the major problems in most of the studies have been the lack of information on the possible effects of medications, the absence of records for all days on which symptoms could have occurred, and the possible concurrence of symptomatic attacks. Investigators who have been able to control some of these variables have found consistent effects of O_3 on asthma (Table 1-20). Their findings have been in accordance with those of some of the earlier, more qualitative studies. Whittemore and Korn (1980) found small increases in the probability of asthma attacks associated with increases of 0.10 ppm in oxidant levels. Zagraniski et al. (1979) reported an increased prevalence rate for respiratory symptoms with approximately 157 $\mu g/m^3$ (0.08 ppm) O_3 in patients with asthma. Linn et al. (1980, 1983) found decreased pulmonary function and increased symptoms in lightly exercising asthmatics exposed to 314 to 333 $\mu g/m^3$ (0.16 to 0.17 ppm) O_3 or greater, regardless of other pollutants. With increased exercise levels, small effects were found at 235 $\mu g/m^3$ (0.12 ppm) O_3. Lebowitz et al. (1982a, 1983) and Lebowitz (1984) showed effects in asthmatics, related also to temperature, at O_3 levels of 102 to 235 $\mu g/m^3$ (0.052 to 0.12 ppm). There have been no consistent findings of symptom aggravation or changes in lung function in patients with other chronic lung diseases besides asthma.

1.12.3 Epidemiological Studies of Effects of Chronic Exposure

Apparent adaptations have been observed under controlled conditions with humans, but this effect would be difficult to demonstrate in community populations. Recent work with animals suggests that the processes involved in adaptation may lead to other, perhaps adverse effects, but no implications for human health can yet be drawn.

Although animal studies indicate that O_3 impairs defenses against infection (Chapter 10), this impairment has not been examined in clinical studies. No positive studies of O_3 effects on acute respiratory illnesses have been reported in human populations. In addition, most studies have yet to address the hypothesis that years or decades of air pollution exposures beginning in childhood, especially among the sensitive, may increase the risk of developing chronic illness (U.S. Environmental Protection Agency, 1978).

The lack of quantitative measures of oxidant levels limits the usefulness of many studies of pollution exposure and mortality. In addition, properly designed studies have not been conducted to address the effects of oxidants on the growth and development of the lung or on the progression of chronic diseases, although the available evidence is consistent with toxicological data indicating that O_3 is not a strong mutagen or a demonstrable carcinogen at ambient concentrations. Most long-term studies have employed average annual levels or have involved broad ranges of pollution; others have used a simple high-oxidant/low-oxidant dichotomy and compared mortality results. Failure to relate mortality to specific levels (and types) of oxidant pollutants makes formulation of exposure-response relationships impossible. Epidemiological identification of chronic effects of air pollution generally requires well-conducted replicated studies of large, well-defined populations over long periods of time, which are not available at this time for O_3 or other photochemical oxidants.

Studies using quantitative measures find that "ozone alerts" occur frequently in association with high temperature. The latter may mask O_3 effects or by itself produce excess mortality in susceptible elderly cardiopulmonary patients. When attempts have been made to distinguish the effects of O_3, no positive relationship has been found with mortality; rather, the effect correlates most closely with elevated temperature.

1.13 SUMMARY OF THE EVALUATION OF INTEGRATED HEALTH EFFECTS DATA

1.13.1 Health Effects in the General Human Population

Controlled human studies of at-rest exposures to O_3 lasting 2 to 4 hr have demonstrated decrements in forced expiratory volume and flow occurring at and above 0.5 ppm of O_3. Airway resistance was not changed at these O_3 concentrations. Breathing O_3 at rest at concentrations < 0.5 ppm did not significantly impair pulmonary function although the occurrence of some O_3-related pulmonary symptoms has been suggested in a number of studies.

One of the principal modifiers of the magnitude of response to O_3 is minute ventilation ($\dot{V}_E$), which increases proportionately with increases in exercise work load. Adjustment by the respiratory system to an increased work load is characterized by increased frequency and depth of breathing. Consequent increases in $\dot{V}_E$ not only increase the overall volume of inhaled pollutant, but such ventilatory patterns also promote a deeper penetration of ozone into the peripheral lung, which is the region most sensitive to ozone and where a greater absorption of ozone will occur. These processes are further enhanced at high work loads ($\dot{V}_E > 35$ L/min), since the mode of breathing will most likely change at that $\dot{V}_E$ from nasal to oronasal.

Even in well-controlled experiments on a homogeneous group of subjects, physiological responses to the same work and pollutant loads will vary widely among individuals. Despite such large interindividual variability, the magnitude of group mean lung function changes is positively associated with the level of exercise and ozone concentration. Based on reported studies of 1 to 3 hr duration, significant pulmonary function impairment (decrement) occurs when exercise is combined with exposure to ozone:

1. Light exercise ($\dot{V}_E \leq 25$ L/min) - Effects at ≥ 0.37 ppm O_3;
2. Moderate exercise ($\dot{V}_E = 26$ to 43 L/min) - Effects at ≥ 0.30 ppm O_3;
3. Heavy exercise ($\dot{V}_E = 44$ to 63 L/min) - Effects at ≥ 0.24 ppm O_3; and
4. Very heavy exercise ($\dot{V}_E \geq 64$ L/min) - Effects at ≥ 0.18 ppm O_3, with suggestions of decrements at 0.12 ppm O_3.

For the majority of the controlled studies, 15-min intermittent exercise alternated with 15-min rest was employed for the duration of the exposure. Continuous exercise equivalent in duration to the sum of intermittent exercise periods at comparable ozone concentrations (0.2 to 0.4 ppm) and minute ventilation (60 to 80 L/min) seems to elicit about the same changes in pulmonary function. The maximum response to O_3 exposure can be observed within 5 to 10 min following the end of each exercise period. Functional recovery, at least from a single exposure with exercise, appears to progress in two phases: during the initial rapid phase, lasting between 1 and 3 hr, pulmonary function improves more than 50 percent; this is followed by a much slower recovery that is usually completed within 24 hr. In some individuals, despite apparent functional recovery, other regulatory systems may still exhibit abnormal responses when stimulated; e.g., airway hyperreactivity might persist for days.

A close association has been observed between changes in pulmonary function and the occurrence of respiratory symptoms in response to acute exposure to O_3. This association holds for both the time-course and magnitude of effects. The symptoms found in association with clinical exposure to O_3 alone and with exposure to photochemical air pollution are similar but not identical. Eye irritation, one of the most common complaints associated with photochemical pollution, is not characteristic of clinical exposures to O_3, even at concentrations several times higher than any likely to be encountered in ambient air. There is also evidence to suggest that other symptoms, indicative of either upper or lower respiratory tract irritation, are more likely to occur in populations exposed to ambient air pollution than in subjects exposed to O_3 alone in chamber studies. For example, cough has been reported at 0.08 ppm O_3 and at 0.10 ppm oxidants in epidemiological studies and during clinical exposure to 0.12 ppm O_3; nose and throat irritation have been reported in community studies in association with 0.10 ppm oxidants but not at or below 0.15 ppm O_3 in laboratory studies. Between 0.15 and 0.30 ppm, a variety of both respiratory and nonrespiratory symptoms have been reported in controlled exposures. They include throat dryness, difficulty or pain during deep inspiration, chest tightness, substernal soreness or pain, wheezing, lassitude, malaise, and nausea. Symptoms are therefore considered to be useful adjuncts in assessing the effects of O_3 and photochemical pollution, particularly if combined with objective measures of lung function.

Only a few studies have been designed to examine the effects of O_3 on exercise performance. In one study, very heavy exercise ($\dot{V}_E$ > 64 L/min) at a high O_3 concentration (0.75 ppm) reduced postexposure maximal exercise capacity by limiting maximal oxygen consumption; submaximal oxygen consumption changes were inconsistent. The extent of ventilatory and respiratory metabolic changes observed during or following the exposure appears to have been related to the magnitude of pulmonary function impairment. Whether such changes are consequent to respiratory discomfort (i.e., symptomatic effects) or are the result of changes in lung mechanics or both is still unclear and needs to be elucidated.

Environmental conditions such as heat and relative humidity may enhance subjective symptoms and physiological impairment following O_3 exposure. Modification of the effects of O_3 by these factors may be attributed to increased ventilation which, like exercise, increases the overall volume of inhaled pollutant and promotes greater penetration into peripheral areas of the lung.

Additional factors suspected of altering sensitivity to ozone are numerous. For example, age differences, especially between the very young and the very old; gender differences, especially for children; personal habits such as cigarette smoking; and possibly social, cultural, or economic factors such as differences in nutritional status or differences in immunological status may predispose individuals to susceptibility to ozone. Those actually known to alter sensitivity, however, are few, largely because they have not been examined adequately to determine definitively their effects on sensitivity to O_3. The following briefly summarizes what is actually known from the data regarding the importance of these factors:

1. Age. Although changes in growth and development of the lung with age have been postulated as one of many factors capable of modifying responsiveness to O_3, studies have not been designed to test adequately for effects of O_3 in different age groups.

2. Sex. Sex differences in responsiveness to ozone have not been adequately studied. Lung function of women, as assessed by changes in $FEV_{1.0}$, appears to be affected more than that of men under similar exercise and exposure conditions, but the differences have not been analyzed systematically. Further research is needed to determine whether differences in lung volumes or differences in exercise capacity during exposure may lead to sex differences in responses to O_3.

3. Smoking Status. Differences between smokers and nonsmokers have been studied often, but the data are not documented well and are often confusing. Published results indicate a discrepancy in findings. There is some evidence, however, to suggest that smokers may be less sensitive to O_3.

4. Nutritional Status. Antioxidant properties of vitamin E in preventing ozone-initiated peroxidation *in vitro* are well demonstrated and their protective effects *in vivo* are clearly demonstrated in rats and mice. No evidence indicates, however, that man would benefit from increased vitamin E intake relative to ambient ozone exposures.

5. Red Blood Cell Enzyme Deficiencies. There have been too few studies performed to document reliably that individuals with a hereditary deficiency of glucose-6-phosphate dehydrogenase may be at-risk to significant hematological effects from O_3 exposure.

Successive daily brief exposures of healthy human subjects to O_3 (<0.7 ppm for approximately 2 hr) induce a typical temporal pattern of response. Maximum functional changes that occur after the first or second exposure day become progressively attenuated on each of the subsequent days. By the fourth day of exposure, the effects are, on the average, not different from those observed following control (air) exposure. Individuals need between 3 and 7 days to develop full attenuation, with more sensitive subjects requiring more time. The magnitude of a peak response to O_3 appears to be directly related to its concentration. In addition, concentrations of O_3 that have no detectable effect appear not to invoke changes in response to subsequent exposures at higher O_3 concentrations. Full attenuation, even in ozone-sensitive subjects, does not persist for more than 3 to 7 days in most individuals, while partial attenuation might persist for up to 2 weeks. Although symptomatic response is generally related to the magnitude of the functional response, partial symptomatic attenuation appears to persist longer, for up to 4 weeks.

Whether populations exposed to photochemical air pollution develop at least partial attenuation is unknown. No epidemiological studies have been designed to test this hypothesis. While there is limited information obtained from controlled laboratory studies to support this hypothesis, additional information is required.

Responses to O_3, whether functional, biochemical, or morphological, have the potential for altering responses in both man and laboratory animals during repeated or continuous exposure. At present, the underlying mechanisms for this response are poorly understood and the effectiveness of such mitigating forces in protecting the long-term health of the individual against O_3 is still uncertain. Therefore, hyperresponsiveness to O_3, including changes in bronchial reactivity, and the subsequent attenuation of responsiveness may be viewed as sequential states in a continuing process.

1.13.2 Health Effects in Potentially Susceptible Individuals

Currently available evidence indicates that individuals with preexisting disease respond to O_3 exposure to a similar degree as normal subjects. Patients with chronic obstructive lung disease and/or asthma have not shown increased sensitivity to O_3 in controlled human exposure studies, but there is some indication from epidemiological studies that asthmatics may be symptomatically and possibly functionally more sensitive than healthy individuals to ambient air exposures. Appropriate inclusion and exclusion criteria for selection of these subjects, however, especially better clinical diagnoses validated by pulmonary function, must be considered before their sensitivity to O_3 can be adequately determined. None of these factors has been sufficiently studied in relation to O_3 exposures to give definitive answers. Thus, estimates of at-risk populations are difficult to assess with any precision.

1.13.3 Extrapolation of Effects Observed in Animals to Human Populations

Several animal experiments have demonstrated increased susceptibility to respiratory infections following O_3 exposure. Thus, it could be hypothesized that humans exposed to O_3 could experience decrements in their host defenses against infection. At the present time, however, these effects have not been described in humans exposed to O_3, so that concentrations at which effects might occur in man or the severity of such effects are unknown and difficult to predict.

Animal studies have also reported a number of extrapulmonary responses to O_3, including cardiovascular, reproductive, and teratological effects, along with changes in endocrine function. The implications of these findings for human health are difficult to judge at the present time. In addition, central nervous system effects, alterations in red blood cell morphology and enzymatic activity, as well as chromosomal effects on circulating lymphocytes, have been observed in man and laboratory animals following exposure to high concentrations of O_3. It is unlikely, however, that these changes would have any functional significance in humans when exposure schedules are used that are representative of exposures that the population at large might actually experience.

Despite wide variations in study techniques and experimental designs, acute and subchronic exposures of animals to levels of ozone < 0.5 ppm produce similar types of responses in all species examined. A characteristic inflammatory lesion occurs at the junction of the conducting airways and the gas-exchange regions of the lung after acute O_3 exposure. Dosimetry model simulations predict that the maximal tissue dose of O_3 occurs in this region of the lung. Continuation of the inflammatory process during longer O_3 exposures is especially important since it appears to be correlated with increased lung collagen content and remodeling of the centriacinar airways. There is no evidence of emphysema, however, in the lungs of animals exposed to O_3 for prolonged periods of time.

Since substantial animal data exists for O_3-induced changes in lung structure and function, biochemistry, and host defenses, it is conceivable that man may experience more types of effects than have been established in human clinical studies. It is important to note, however, that this is a qualitative probability; it does not permit assessment of the ozone concentrations at which man might experience similar effects.

1.13.4 Health Effects of Other Photochemical Oxidants and Pollutant Mixtures

Controlled human and animal exposures have not consistently demonstrated any enhancement of respiratory effects for combined exposures of O_3 with SO_2, NO_2, CO, or H_2SO_4 and other particulate aerosols. Ozone alone is considered to be responsible for the observed effects of those combinations or of multiple mixtures of these pollutants. In addition, there have been far too few controlled toxicological studies with other oxidants, such as peroxyacetyl nitrate or hydrogen peroxide, to permit any sound scientific evaluation of their contribution to the toxic action of photochemical oxidant mixtures. Nevertheless, there is still some concern that combinations of oxidant pollutants with other pollutants may contribute to the symptom aggravation and decreased lung function described in epidemiological studies on individuals with asthma and in children and young adults. For this reason, the effects of interaction between inhaled oxidant gases and other environmental pollutants on the lung need to be systematically studied using exposure regimens that are more closely representative of ambient air ratios of peak concentrations, frequency, duration, and time intervals between events.

1.13.5 Identification of Potentially At-Risk Populations or Subpopulations

Despite uncertainties that may exist in the data, it is possible to identify three major subpopulations that may be at particular risk from exposure to ozone, based on known health effects, activity patterns, personal habits, and actual or potential exposures to ozone.

The first major subpopulation that appears to be at particular risk from exposure to ozone is that subgroup of the general population characterized as having preexisting disease. Available data on actual differences in sensitivity between these and healthy, normal members of the general population indicate that under the exposure regimes used to date individuals with preexisting disease may not be more sensitive to ozone than normal individuals.

Nevertheless, two considerations place these individuals among subpopulations at potential risk from exposure to ozone. First, it must be noted that concern with triggering untoward reactions has necessitated the use of low concentrations and low exercise levels in most studies on subjects with preexisting disease. Therefore, few or no data on responses at higher concentrations and higher exercise levels are available for comparison with responses in normal subjects. Thus, definitive data on responses in individuals with preexisting disease are not available and may not ever become available. Second, however, it must be emphasized that in individuals with already compromised pulmonary function, the decrements in function produced by exposure to ozone, while similar to or even the same as those experienced by normal subjects, represent a further decline in volumes and flows that are already diminished. Such declines may be expected to impair further the ability to perform normal activities. In individuals with preexisting diseases such as asthma or allergies, increases in symptoms upon exposure to ozone, above and beyond symptoms seen in the general population, may also impair or further curtail the ability to function normally.

A second major subpopulation at apparent special risk from exposure to ozone consists of individuals ("responders") in the general population, not yet characterized medically except for their responses to ozone, who experience greater decrements in lung function from exposure to ozone than those observed in the remainder of the general population. As yet no means of determining in advance those members of the general population who are "responders" has been devised.

Data presented in this chapter underscore the importance of exercise in the potentiation of effects from exposure to ozone. Thus, a third major subpopulation potentially at risk from exposure to ozone is composed of those individuals (healthy and otherwise) whose activities out of doors, whether vocational or avocational, result in increases in minute ventilation. Although many individuals with preexisting disease would not be expected to exercise at the same levels one would expect in healthy individuals, any increase in activity level would bring about a commensurate increase in minute ventilation. To the extent that the aged, the young, males, or females participate in activities out of doors that raise their minute ventilations, all of these subgroups may be considered to be potentially at risk, depending upon other determinants of total ozone dose, O_3 concentration, and exposure duration.

Other biological and nonbiological factors are suspected of influencing responses to ozone. Data remain inconclusive at the present, however, regarding the importance of age, gender, and other factors in influencing response to ozone. Thus, at the present time, no other subpopulations are thought to be biologically predisposed to increased sensitivity to ozone. It must be emphasized, however, that the final identification of those effects that are considered "adverse" and the final identification of "at-risk" populations are both the domain of the Administrator.

1.14 REFERENCES

Abraham, W. M.; Lauredo, I.; Sielczak, M.; Yerger, L.; King, M. M.; Ratzan, K. (1982) Enhancement of bacterial pneumonia in sheep by ozone exposure. Am. Rev. Respir. Dis. Suppl. 125(4 pt. 2): 148.

Abraham, W. M.; Januszkiewicz, A. J.; Mingle, M.; Welker, M.; Wanner, A.; Sackner, M. A. (1980) Sensitivity of bronchoprovocation and tracheal mucous velocity in detecting airway responses to O_3. J. Appl. Physiol. Respir. Environ. Exercise Physiol. 48: 789-793.

Adams, W. C.; Schelegle, E. S. (1983) Ozone toxicity effects consequent to prolonged, high intensity exercise in trained endurance athletes. J. Appl. Physiol. Respir. Environ. Exercise Physiol. 55: 805-812.

Adedipe, N. O.; Barrett, R. E.; Ormrod, D. P. (1972) Phototoxicity and growth responses of ornamental bedding plants to ozone and sulfur dioxide. J. Am. Soc. Hort. Sci. 97: 341-345.

Adedipe, N. O.; Ormrod, D. P. (1974) Ozone induced growth suppression in radish plants in relation to pre- and post-fumigation temperatures. Z. Pflanzen Physiol., 71: 281-287.

Aharonson, E. F.; Menkes, H.; Gurtner, G.; Swift, D. L.; Proctor, D. F. (1974) Effect of respiratory airflow rate on removal of soluble vapors by the nose. J. Appl. Physiol. 27: 654-657.

Allen, A. O.; Hochanadel, C. J.; Ghormley, J. A.; Davis, T. W. (1952) Decomposition of water and aqueous solutions under mixed fast-neutron and γ-radiation. J. Phys. Chem. 56: 575-586.

Alpert, S. M.; Gardner, D. E.; Hurst, D. J.; Lewis, T. R.; Coffin, D. L. (1971b) Effects of exposure to ozone on defensive mechanisms of the lung. J. Appl. Physiol. 31: 247-252.

Alpert, S. M.; Schwartz, B. B.; Lee, S. D.; Lewis, T. R. (1971a) Alveolar protein accumulation. A sensitive indicator of low level oxidant toxicity. Arch. Intern. Med. 128: 69-73.

Altshuller, A. P. (1983) Measurements of the products of atmospheric photochemical reactions in laboratory studies and in ambient air--relationships between ozone and other products. Atmos. Environ. 17: 2383-2427.

Altshuller, A. P.; McPherson, S. P. (1963) Spectrophotometric analysis of aldehydes in the Los Angeles atmosphere. J. Air Pollut. Control Assoc. 13:109-111.

Amdur, M. O.; Ugro, V.; Underhill, D. W. (1978) Respiratory response of guinea pigs to ozone alone and with sulfur dioxide. Am. Ind. Hyg. Assoc. J. 39: 958-961.

Amoruso, M. A.; Witz, G.; Goldstein, B. D. (1981) Decreased superoxide anion radical production by rat alveolar macrophages following inhalation of ozone or nitrogen dioxide. Life Sci. 28: 2215-2221.

Andreae, W. A. (1955) A sensitive method for the estimation of hydrogen peroxide in biological materials. Nature (London) 175: 859-860.

Aranyi, C., Vana, S. C.; Thomas, P. T.; Bradof, J. N.; Fenters, J. D.; Graham, J. A.; Miller, F. J. (1983) Effects of subchronic exposure to a mixture of O_3, SO_2 and $(NH_4)_2SO_4$ on host defenses of mice. J. Toxicol. Environ. Health 12: 55-71.

Armstrong, W. A.; Humphreys, W. G. (1965) A L.E.T. independent dosimeter based on the chemiluminescent determination of H_2O_2. Can. J. Chem. 43: 2576.

Atkinson, R.; Aschmann, S. M.; Fitz, D. R.; Winer, A. M.; Pitts, J. N., Jr. (1982) Rate constants for the gas-phase reactions of O_3 with selected organics at 296 K. Int. J. Chem. Kinet. 14: 13-18.

Atkinson, R.; Aschmann, S. M.; Winer, A. M.; Pitts, J. N., Jr. (1981) Rate constants for the gas-phase reactions of O_3 with a series of carbonyls at 296 K. Int. J. Chem. Kinet. 13: 1133-1142.

Atkinson, R.; Aschmann, S. M.; Winer, A. M.; Pitts, J. N., Jr. (1984c) Kinetics of the gas phase reactions of NO_3 radicals with a series of dialkenes, cycloalkenes and monoterpenes at 295 ± 1 K. Environ. Sci. Technol. (in press).

Atkinson, R.; Carter, W. P. L. (1984) Kinetics and mechanisms of the reactions of ozone with organic compounds in the gas phase, submitted to Chem. Rev.

Atkinson, R.; Carter, W. P. L.; Plum, C. N.; Winer, A. M.; Pitts, J. N., Jr. (1984d) Kinetics of the gas phase reactions of NO_3 radicals with a series of aromatics at 296 ± 2 K. Int. J. Chem. Kinet. (in press).

Atkinson, R.; Darnall, K. R.; Lloyd, A. C.; Winer, A. M.; Pitts, J. N., Jr. (1979) Kinetics and mechanisms of the reactions of the hydroxyl radical with organic compounds in the gas phase. Adv. Photochem. 11: 375-488.

Atkinson, R.; Darnall, K. R.; Pitts, J. N., Jr. (1978) Rate constants for the reactions of OH radicals and ozone with cresols at 300 ± 1 K. J. Phys. Chem. 82: 2759-2761.

Atkinson, R.; Lloyd, A. C. (1984) Evaluation of kinetic and mechanistic data for modeling of photochemical smog. J. Phys. Chem. Ref. Data (in press).

Atkinson, R.; Pitts, J. N., Jr.; Aschmann, S. M. (1984b) Tropospheric reactions of dimethyl sulfide with NO_3 and OH radicals. J. Phys. Chem. (in press).

Atkinson, R.; Plum, C. N.; Carter, W. P. L.; Winer, A. M.; Pitts, J. N., Jr. (1984a) Rate constants for the gas phase reactions of NO_3 radicals with a series of organics in air at 298 ± 1 K. J. Phys. Chem. (in press).

Atwal, O. S.; Pemsingh, R. S. (1981) Morphology of microvascular changes and endothelial regeneration in experimental ozone-induced parathyroiditis. Am. J. Pathol. 102: 297-307.

Atwal, O. S.; Samagh, B. S.; Bhatnagar, M. K. (1975) A possible autoimmune parathyroiditis following ozone inhalation. II. A histopathologic, ultrastructural, and immunofluorescent study. Am. J. Pathol. 80: 53-68.

Atwal, O. S.; Wilson, T. (1974) Parathyroid gland changes following ozone inhalation. A morphologic study. Arch. Environ. Health 28: 91-100.

Barry, B. E.; Miller, F. J.; Crapo, J. D. (1983). Alveolar epithelial injury caused by inhalation of 0.25 ppm of ozone. In: Lee, S. D.; Mustafa, M. G.; Mehlman, M. A., eds. International symposium on the biomedical effects of ozone and related photochemical oxidants; March 1982; Pinehurst, NC. Princeton, NJ: Princeton Scientific Publishers, Inc; pp. 299-309. (Advances in modern environmental toxicology: v. 5.)

Bartlett, D.; Faulkner, C. S. II; Cook, K. (1974) Effect of chronic ozone exposure on lung elasticity in young rats. J. Appl. Physiol. 37: 92-96.

Bass, A. M.; Ledford, A. E., Jr.; Whittaker, J. K. (1977) Ultraviolet photometer for ozone calibration. In: Dimitriades, B., ed. International Conference on Photochemical Oxidant Pollution and Its Control; January. Volume I. Research Triangle Park, NC: U.S. Environmental Protection Agency; pp. 13-17; EPA report no. EPA-600/3-77-001a.

Beloin, N. J. (1972) A field study: fading of dyed fabrics by air pollution. Text. Chem. Color. 4: 77-78.

Beloin, N. J. (1973) Fading of dyed fabrics by air pollutants: a chamber study. Text. Chem. Color. 5: 128-133.

Bennett, J. H. (1979) Foliar exchange of gases. In: Heck, W. W.; Krupa, S. K.; and Linzon, S. N., Eds. Handbook of Methodology for the Assessment of Air Pollution Effects on Vegetation. Air Pollution Control Association, Pittsburgh. pp. 10-1 to 10-29.

Bennett, J. P.; Oshima, R. J.; Lippert, L. F. (1979) Effects of ozone on injury and dry matter partitioning in pepper plants. Environ. Exp. Bot., 19: 33-39.

Benoit, L. F.; Skelly, J. M.; Moore, L. D.; Dochinger, L. S. (1982) Radial growth reductions in Pinus strobus L. correlated with foliar ozone sensitivity as an indicator of ozone induced losses in eastern forests. Can. J. For. Res., 12: 673-678.

Benoit, L. F.; Skelly, J. M.; Moore, L. D.; Dochinger, L. S. (1982) Radial growth reductions of Pinus strobus L. correlated with foliar ozone sensitivity as an indicator of ozone-induced losses in eastern forests. Can. J. For. Res. 12: 673-678.

Bergers, W. W. A.; Gerbrandy, J. L. F.; Stap, J. G.; Dura, E. A. (1983) Influence of air polluting components viz. ozone and the open air factor on host-resistance towards respiratory infections. In: Lee, S. D.; Mustafa, M. G.; Mehlman, M. A., eds. International symposium on the biomedical effects of ozone and related photochemical oxidants; March 1982; Pinehurst, NC. Princeton, NJ: Princeton Scientific Publishers, Inc.; pp. 459-467. (Advances in modern environmental toxicology: vol. 5).

Berk, J. V.; Young, R. A.; Brown, S. R.; Hollowell, C. D. (1981) Impact of energy-conserving retrofits on indoor air quality in residential housing. Presented at the 74th Annual Meeting of the Air Pollution Control Association; June; Philadelphia, PA. Berkeley, CA: University of California, Lawrence Berkeley Laboratory; report no. LBL-12189. Cited in: Yocom, J. E. (1982).

Berliner, J. A.; Kuda, A.; Mustafa, M. G.; Tierney, D. F. (1978) Pulmonary morphologic studies of ozone tolerance in the rat (a possible mechanism for tolerance). Scanning Electron Microsc. 2: 879-884.

Berry, C. R.; Ripperton, L. A. (1963) Ozone, a possible cause of white pine emergence tipburn. Phytopathology 53: 552-557.

Bhatnagar, R. S.; Hussain, M. Z.; Sorensen, K. R.; Mustafa, M. G.; von Dohlen, F. M.; Lee, S. D. (1983) Effect of ozone on lung collagen biosynthesis. In: Lee, S. D.; Mustafa, M. G.; Mehlman, M. A., eds. International symposium on the biomedical effects of ozone and related photochemical oxidants; March 1982; Pinehurst, N.C. Princeton, NJ: Princeton Scientific Publishers, Inc.; pp. 311-321. (Advances in modern environmental toxicology: vol. 5).

Billings, W. D. (1978) Plants and the ecosystem. 3rd Edition. Belmont, CA: Wadsworth Publishing Company, Inc.; pp. 1-62.

Blum, U. T.; Smith, G. R.; and Fites, R. C. (1982) Effects of multiple O_3 exposures on carbohydrate and mineral contents of Ladino clover. Environ. Exp. Bot., 22: 143-154.

Boatman, E. S.; Sato, S.; Frank, R. (1974) Acute effects of ozone on cat lungs. II. Structural. Am. Rev. Respir. Dis. 110: 157-169.

Boche, R. D.; Quilligan, J. J., Jr. (1960) Effects of synthetic smog on spontaneous activity of mice. Science (Washington, DC) 131: 1733-1734.

Bogaty, H.; Campbell, K. S.; Appel, W. D. (1952) The oxidation of cellulose by ozone in small concentrations. Text. Res. J. 22: 81-83.

Bollinger, M. J.; Parrish, D. D.; Hahn, C.; Albritton, D. L.; Fehsenfeld, F. C. (1982) NO_x measurements in clean continental air. In: Proceedings of 2nd Symposium on Composition of the Nonurban Troposphere; May; Williamsburg, VA.

Boorman, G. A.; Schwartz, L. W.; Dungworth, D. L. (1980) Pulmonary effects of prolonged ozone insult in rats. Morphometric evaluation of the central acinus. Lab. Invest. 43: 108-115.

Boorman, G. A.; Schwartz, L. W.; McQuillen, N. K.; Brummer, M. E. (1977) Pulmonary response following long-term intermittent exposure to ozone: structural and morphological changes. Am. Rev. Respir. Dis. 115: 201.

Bormann, F. H.; Smith, W. H. (1980) Effects of air pollution on forest ecosystems. In: Energy and the fate of ecosystems. Washington, DC: National Academy of Sciences; pp. 308-318.

Bowman, L. D.; Horak, R. F. (1972) A continuous ultraviolet absorption ozone photometer. Anal. Instrum. 10: 103-108.

Bradley, C. E.; Haagen-Smit, A. J. (1951) The application of rubber in the quantitative determination of ozone. Rubber Chem. Technol. 24: 750-775.

Bradley, M. O.; Erickson, L. C. (1981) Comparison of the effects of hydrogen peroxide and x-ray irradiation on toxicity, mutation, and DNA damage/ repair in mammalian cells (V-79). Biochim. Biophys. Acta 654: 135-141.

Bradley, M. O.; Hsu, I.C.; Harris, C.C. (1979) Relationships between sister chromatid exchange and mutagenicity, toxicity, and DNA damage. Nature (London) 282: 318-320.

Breeding, R. J.; Lodge, J. P., Jr.; Pate, J. B.; Sheesley, D. C.; Klonis, H. B.; Fogle, B.; Anderson, J. A.; Englert, T. R.; Haagenson, P. L.; McBeth, R. B.; Morris, A. L.; Pogue, R.; Wartburg, A. F. (1973) Background trace gas concentration in the central United States. J. Geophys. Res. 78: 7057-7064.

Brewer, A. W.; Milford, J. R. (1960) The Oxford Kew ozone sonde. Proc. R. Soc. London Ser. A256: 470-495.

Brinkman, R.; Lamberts, H.; Veninga, T. (1964) Radiomimetic toxicity of ozonized air. Lancet 1: 133-136.

Bruckmann, P. W.; Willner, H. (1983) Infrared spectroscopic study of peroxyacetyl nitrate (PAN) and its decomposition products. Environ. Sci. Technol. 17: 352-357.

Brummer, M. E. G.; Schwartz, L. W.; McQuillen, N. K. (1977) A quantitative study of lung damage by scanning electron microscopy. Inflammatory cell response to high-ambient levels of ozone. Scanning Electron Microsc. 2: 513-518.

Bufalini, J. J.; Gay, B. W., Jr.; Brubaker, K.L. (1972) Hydrogen peroxide formation from formaldehyde photooxidation and its presence in urban atmospheres. Environ. Sci. Technol. 6: 816-821.

Burton, C. S.; Bekowies, P. J.; Pollack, R. I.; Connell, P. (1976) Oxidant/ ozone ambient measurement methods: an assessment and evaluation. EF76-111R, Systems Applications, Inc., San Rafael, CA. August.

California Air Resources Board. (1976) A study of the effect of atmospheric humidity on analytical oxidant measurement methods. Presented at the 15th Conference on Methods in Air Pollution Studies, J. J. Wesolowski, Chairman, California Air Resources Board, Air and Industrial Hygiene Laboratory, Berkeley, CA.

California Air Resources Board. (1978) California Air Quality Data: July-August-September. 10(13): 2-3. Available from Technical Service Div., California Air Resources Board, Sacramento, CA.

Campbell, G. G.; Schurr, G. G.; Slawikowski, D. E.; Spence, J. W. (1974) Assessing air pollution damage to coatings. J. Paint Technol. 46: 59-71.

Campbell, K. I.; Clarke, G. L.; Emik, L. O.; Plata, R. L. (1967) The atmospheric contaminant peroxyacetyl nitrate. Arch. Environ. Health 15: 739-744.

Campbell, K. I.; Hilsenroth, R. H. (1976) Impaired resistance to toxin in toxoid-immunized mice exposed to ozone on nitrogen dioxide. Clin. Toxicol. 9: 943-954.

Carter, W. P. L.; Winer, A. M.; Pitts, J. N., Jr. (1981) Major atmospheric sink for phenol and the cresols. Reaction with the nitrate radical. Environ. Sci. Technol. 15: 829-830.

Castleman, W. L.; Dungworth, D. L.; Schwartz, L. W.; Tyler, W. S. (1980) Acute respiratory bronchiolitis: an ultrastructural and autoradiographic study of epithelial cell injury and renewal in rhesus monkeys exposed to ozone. Am. J. Pathol. 98: 811-840.

Castleman, W. L.; Dungworth, D. L.; Tyler, W. S. (1973) Cytochemically detected alterations of lung acid phosphatase reactivity following ozone exposure. Lab. Invest. 29: 310-319.

Castleman, W. L.; Tyler, W. S.; Dungworth, D. L. (1977) Lesions in respiratory bronchioles and conducting airways of monkeys exposed to ambient levels of ozone. Exp. Mol. Pathol. 26: 384-400.

Cavender, F. L.; Steinhagen, W. H.; Ulrich, C. E.; Busey, W. M.; Cockrell, B. Y.; Haseman, J. K.; Hogan, M. D.; Drew, R. T. (1977) Effects in rats and guinea pigs of short-term exposures to sulfuric acid mist, ozone, and their combination. J. Toxicol. Environ. Health 3: 521-533.

Chock, D. P.; Kumar, S.; Herrmann, R. W. (1982) An analysis of trends in oxidant air quality in the South Coast Air Basin of California. Atmos. Environ. 16: 2615-2624.

Chow, C. K. (1976) Biochemical responses in lungs of ozone-tolerant rats. Nature (London) 260: 721-722.

Chow, C. K.; Cross, C. E.; Kaneko, J. J. (1977) Lactate dehydrogenase activity and isoenzyme pattern in lungs, erythrocytes, and plasma of ozone-exposed rats and monkeys. J. Toxicol. Environ. Health 3: 877-884.

Chow, C. K.; Dillard, C. J.; Tappel, A. L. (1974) Glutathione peroxidase system and lysozyme in rats exposed to ozone or nitrogen dioxide. Environ. Res. 7: 311-319.

Chow, C. K.; Hussain, M. Z.; Cross, C. E.; Dungworth, D. L.; Mustafa, M. G. (1976) Effect of low levels of ozone on rat lungs. I. Biochemical responses during recovery and reexposure. Exp. Mol. Pathol. 25: 182-188.

Chow, C. K.; Kaneko, J. J. (1979) Influence of dietary vitamin E on the red cells of ozone-exposed rats. Environ. Res. 19: 49-55.

Chow, C. K.; Mustafa, M. G.; Cross, C. E.; Tarkington, B. K. (1975) Effects of ozone exposure on the lungs and the erythrocytes of rats and monkeys: relative biochemical changes. Environ. Physiol. Biochem. 5: 142-146.

Chow, C. K.; Plopper, C. G.; Chiu, M.; Dungworth, D. L. (1981) Dietary vitamin E and pulmonary biochemical and morphological alterations of rats exposed to 0.1 ppm ozone. Environ. Res. 24: 315-324.

Chow, C. K.; Tappel, A. L. (1972) An enzymatic protective mechanism against lipid peroxidation damage to lungs of ozone-exposed rats. Lipids 7: 518-524.

Chow, C. K.; Tappel, A. L. (1973) Activities of pentose shunt and glycolytic enzymes in lungs of ozone-exposed rats. Arch. Environ. Health 26: 205-208.

Christensen, E.; Giese, A. C. (1954) Changes in absorption spectra of nucleic acids and their derivatives following exposure to ozone and ultraviolet radiation. Arch. Biochem. Biophys. 51: 208-216.

Clark, K. W.; Posin, C. I.; Buckley, R. D.. (1978) Biochemical response of squirrel monkeys to ozone. J. Toxicol. Environ. Health 4: 741-753.

Clemons, G. K.; Garcia, J. F. (1980a) Endocrine aspects of ozone exposure in rats. Arch. Toxicol. Suppl. (4): 301-304.

Clemons, G. K.; Garcia, J. F. (1980b) Changes in thyroid function after short-term ozone exposure in rats. J. Environ. Pathol. Toxicol. 4: 359-369.

Cleveland, W. S.; Graedel, T. E.; Kleiner, B. (1976) Photochemical air pollution: transport from the New York City area into Connecticut and Massachusetts. Science (Washington, DC) 191: 179-181.

Coffin, D. L.; Blommer, E. J. (1970) Alteration of the pathogenic role of streptococci group C in mice conferred by previous exposure to ozone. In: Silver, I. H., ed. Aerobiology: proceedings of the third international symposium; September 1969; Sussex, England. New York: Academic Press, Inc.; pp. 54-61.

Coffin, D. L.; Gardner, D. E. (1972a) The role of tolerance in protection of the lung against secondary insults. In: MEDICHEM: first international symposium of occupational physicians of the chemical industry; April; Ludwigshafen, West Germany. Ludwigshafen, West Germany: Badische Anilin-und Soda-Fabrik (BASF); pp. 344-364.

Coffin, D. L.; Gardner, D. E. (1972b) Interaction of biological agents and chemical air pollutants. Ann. Occup. Hyg. 15: 219-235.

Coffin, D. L.; Gardner, D. E.; Holzman, R. S.; Wolock, F. J. (1968) Influence of ozone on pulmonary cells. Arch. Environ. Health 16: 633-636.

Cohen, I. R.; Purcell, T. C.; Altshuller, A. P. (1967) Analyses of the oxidant in photooxidation reactions. Environ. Sci. Technol. 1: 247-252.

Costa, D. L.; Kutzman, R. S.; Lehmann, J. R.; Popenoe, E. A.; Drew, R. T. (1983) A subchronic multi-dose ozone study in rats. In: Lee, S. D.; Mustafa, M. G.; Mehlman, M. A., eds. International symposium on the biomedical effects of ozone and related photochemical oxidants; March 1982; Pinehurst, NC. Princeton, NJ: Princeton Scientific Publishers, Inc.; pp. 369-393. (Advances in modern environmental toxicology: v. 5).

Cox, G. W.; Atkins, M. D. (1979) Agricultural ecology: an analysis of world food production systems. San Francisco, CA: W.H. Freeman and Co.; pp. 35-38.

Cronn, D. R. (1982) Monitoring of ambient halocarbons and natural hydrocarbons in the Smoky Mountains. In: Proceedings from 2nd Symposium on Composition of the Nonurban Troposphere; May; Williamsburg, VA.

Csanyi, L. J. (1981) Analytical applications of mixed-ligand complexes. III. Vanadium (V)-xylenol orange reagent mixture for the spectrophotometric determination of traces of hydrogen peroxide. Microchem. J. 26: 10-16.

Darley, E. F.; Kettner, K. A.; Stephens, E. R. (1963) Analysis of peroxyacyl nitrates by gas chromatography with electron capture detection. Anal. Chem. 35: 589-591.

Davies, K. M. (1979) Influence of environmental factors on interply adhesion. In: Proceedings of the International Rubber Conference; pp. 80-89.

DeLucia, A. J.; Hogue, P. M.; Mustafa, M. G.; Cross, C. E. (1972) Ozone interaction with rodent lung, effect on sulfhydryls and sulfhydryl-containing enzyme activities. J. Lab. Clin. Med. 80: 559-566.

DeLucia, A. J.; Mustafa, M. G.; Cross, C. E.; Plopper, C. G.; Dungworth, D. L.; Tyler, W. S. (1975) Biochemical and morphological alterations in the lung following ozone exposure. In: Rai, C.; Spielman, L. A., eds. Air: I. pollution control and clean energy; 1973; New Orleans, LA; Detroit, MI; Philadelphia, PA; Vancouver, British Columbia. New York, NY: American Institute of Chemical Engineers; pp. 93-100. (AIChE symposium series: no. 147, v. 71).

Demore, W. B.; Patapoff, M. (1976) Comparison of ozone determinations by ultraviolet photometry and gas-phase titration. Environ. Sci. Technol. 10: 897-899.

Demore, W. B.; Romanovsky, J. C.; Feldstein, M.; Hamming, W. J.; Mueller, P. K. (1976) Interagency comparison of iodometric methods for ozone determination. In: Calibration in Air Monitoring. Philadelphia, PA: American Soceity for Testing and Materials; pp. 131-143; ASTM Special Technical Publication 598.

Dietz, W. A. (1967) Response factors for gas chromatographic analyses. J. Gas Chromatogr. 5:68-71.

Dillard, C. J.; Urribarri, N.; Reddy, K.; Fletcher, B.; Taylor, S.; de Lumen, B.; Langberg, S.; Tappel, A. L. (1972) Increased lysosomal enzymes in lungs of ozone-exposed rats. Arch. Environ. Health 25: 426-431.

Dimeo, M. J.; Glenn, M. G.; Holtzman, M. J.; Sheller, J. R.; Nadel, J. A.; Boushey, H. A. (1981) Threshold concentration of ozone causing an increase in bronchial reactivity in humans and adaptation with repeated exposures. Am. Rev. Respir. Dis. 124: 245-248.

Dochinger, L. S.; and Townsend, A. M. (1979) Effects of roadside deicer salts and ozone on red maple progenies. Environ. Pollut., 19: 229-237.

Dorsey, A. P.; Morgan, D. L.; Menzel, D. B. (1983) Filterability of erythrocytes from ozone-exposed mice. In: Abstracts of the third international congress on toxicology; September; San Diego, CA. Toxicol. Lett. 18(suppl. 1): 146.

Dowell, A. R.; Lohrbauer, L. A.; Hurst, D.; Lee, S. D. (1970) Rabbit alveolar macrophage damage caused by in vivo ozone inhalation. Arch. Environ. Health 21: 121-127.

Dubeau, H.; Chung, Y. S. (1979) Ozone response in wild type and radiation-sensitive mutants of Saccharomyces cerevisiae. Mol. Gen. Genet. 176: 393-398.

Dubeau, H.; Chung, Y. S. (1982) Genetic effects of ozone induction of point mutations and genetic recombination in Saccharomyces cerevisiae. Mutat. Res. 102: 249-259.

Duce, R. A.; Mohnen, V. A.; Zimmerman, P. R.; Grosjean, D.; Cautreels, W.; Chatfield, R. B.; Jaenicke, R.; Ogren, J. A.; Pellizzari, E. D.; Wallace, G. T. (1983) Organic material in the global troposphere. Rev. Geophys. Space Phys. 21: 921-952.

Duchelle, S. F.; Skelly, J. M. (1981) Response of common milkweed to oxidant air pollution in the Shenandoah National Park in Virginia. Plant Disease 65: 661-662.

Duchelle, S. F.; Skelly, J. M.; Sharick, T. L.; Chevone, B. I.; Yang, Y. S.; Nellessen, J. E. (1983) Effects of ozone on the productivity of natural vegetation in a high meadow of the Shenandoah National Park of Virginia. J. Environ. Manage. 17: 299-308.

Dungworth, D. L. (1976) Short-term effects of ozone on lungs of rats, mice and monkeys. EHP Environ. Health Perspect. 16: 179.

Dungworth, D. L.; Castleman, W. L.; Chow, C. K.; Mellick, P. W.; Mustafa, M. G.; Tarkington, B.; Tyler, W. S. (1975b) Effects of ambient levels of ozone on monkeys. Fed. Proc. Fed. Am. Soc. Exp. Biol. 34: 1670-1674.

Dungworth, D. L.; Clarke, G. L.; Plata, R. L. (1969) Pulmonary lesions produced in A-strain mice by exposure to peroxyacetylnitrates. Am. Rev. Respir. Dis. 99: 565-574.

Dungworth, D. L.; Cross, C. E.; Gillespie, J. R.; Plopper, C. G. (1975a) The effects of ozone on animals. In: Murphy, J. S.; Orr, J. R., eds. Ozone chemistry and technology. A review of the literature: 1961-1974. Philadelphia, PA: The Franklin Institute Press; pp. 29-54.

Easton, R. E.; Murphy, S. D. (1967) Experimental ozone preexposure and histamine. Arch. Env. Health 15: 160-166.

Eaton, W. C.; Decker, C. E.; Tommerdahl, J. B.; Dimmock, F. E. (1979) Study of the nature of ozone, oxides of nitrogen, and nonmethane hydrocarbons in Tulsa, Oklahoma. Research Triangle Park, NC: Environmental Protection Agency; EPA report no. EPA-450/4-79-008a.

Edwards, D. C.; Storey, E. B. (1959) A quantitative ozone test for small specimens. Chem. Can. 11: 34-38.

Ehrlich, R. (1980) Interaction between environmental pollutants and respiratory infections. EHP Environ. Health Perspect. 35: 89-100.

Ehrlich, R. (1983) Changes in susceptibility to respiratory infection caused by exposure to photochemical oxidant pollutants. In: Lee, S. D.; Mustafa, M. G.; Mehlman, M. A., eds. International symposium on the biomedical effects of ozone and related photochemical oxidants; March 1982; Pinehurst, NC. Princeton, NJ: Princeton Scientific Publishers, Inc.; pp. 273-285. (Advances in modern environmental toxicology: v.5).

Ehrlich, R.; Findlay, J. C.; Fenters, J. D.; Gardner, D. E. (1977) Health effects of short-term inhalation of nitrogen dioxide and ozone mixtures. Environ. Res. 14: 223-231.

Ehrlich, R.; Findlay, J. C.; Gardner, D. E. (1979) Effects of repeated exposures to peak concentrations of nitrogen dioxide and ozone on resistance to streptococcal pneumonia. J. Toxicol. Environ. Health 5: 631-642.

Elsayed, N. M.; Hacker, A. D.; Kuehn, K.; Mustafa, M. G.; Schrauzer, G. N. (1983) Dietary antioxidants and the biochemical response to oxidant inhalation. II. Influence of dietary selenium on the biochemical effects of ozone exposure in mouse lung. Toxicol. Appl. Pharmacol. 71: 398-406.

Elsayed, N. M.; Mustafa, M. G.; Postlethwait, E. M. (1982a) Age-dependent pulmonary response of rats to ozone exposure. J. Toxicol. Environ. Health 9: 835-848.

Elsayed, N.; Hacker, A.; Mustafa, M.; Kuehn, K.; Schrauzer, G. (1982b) Effects of decreased glutathione peroxidase activity on the pentose phosphate cycle in mouse lung. Biochem. Biophys. Res. Commun. 104: 564-569.

Erdman, H. E.; Hernandez, T. (1982) Adult toxicity and dominant lethals induced by ozone at specific stages in spermatogenesis in Drosophila virilis. Environ. Mutagen. 4: 657-666.

Eustis, S. L.; Schwartz, L. W.; Kosch, P. C.; Dungworth, D. L. (1981) Chronic bronchiolitis in nonhuman primates after prolonged ozone exposure. Am. J. Pathol. 105: 121-137.

Evans, G.; Finkelstein, P.; Martin, B.; Possiel, N.; Graves, M. (1982) The National Air Pollution Background Network, 1976-1980. Research Triangle Park, NC: U.S. Environmental Protection Agency; EPA report no. EPA-600/4-82-058.

Evans, M. J.; Johnson, L. V.; Stephens, R. J.; Freeman, G. (1976b) Cell renewal in the lungs of rats exposed to low levels of ozone. Exp. Mol. Pathol. 24: 70-83.

Evans, M. J.; Johnson, L. V.; Stephens, R. J.; Freeman, G. (1976a) Renewal of the terminal bronchiolar epithelium in the rat following exposure to NO_2 or O_3. Lab. Invest. 35: 246-257.

Evans, M. J.; Mayr, W.; Bils, R. F.; Loosli, C. G. (1971) Effects of ozone on cell renewal in pulmonary alveoli of aging mice. Arch. Environ. Health 22: 450-453.

Fabbri, L. M.; Aizawa, H.; Alpert, S. E.; Walters, E. H.; O'Byrne, P. M.; Gold, B. D.; Nadel, J. A.; Holtzman, M. J. (1984) Airway hyperresponsiveness and changes in cell counts in bronchoalveolar lavage after ozone exposure in dogs. Am. Rev. Respir. Dis. 129: 288-291.

Fabbri, L.; Mapp, C.; Rossi, A.; Sarto, F.; Trevisan, A.; De Rosa, E. (1979) Pulmonary function changes due to low level occupational exposure to ozone. Med. Lav. 70: 307-312.

Fairchild, E. J. (1967) Tolerance mechanisms: determination of lung responses to injurious agents. Arch. Environ. Health 14: 111-126.

Farmer, J. C.; Dawson, G. A. (1982) Condensation sampling of soluble atmospheric trace gases. J. Geophys. Res. 87: 8931-8942.

Farrell, B. P.; Kerr, H. D.; Kulle, T. J.; Sauder, L. R.; Young, J. L. (1979) Adaptation in human subjects to the effects of inhaled ozone after repeated exposure. Am. Rev. Respir. Dis. 119: 725-730.

Feder, W. A.; Campbell, F. J. (1968) Influence of low levels of ozone on flowering of carnations. Phytopathology. 58: 1038-1039.

Ferman, M. A. (1981) Rural nonmethane hydrocarbon concentrations and composition. In: Bufalini, J. J.; Arnts, R. R., eds. Atmospheric Biogenic Hydrocarbons. Ann Arbor, MI: Ann Arbor Science Publishers, Inc.

Fetner, R. H. (1962) Ozone-induced chromosome breakage in human cell cultures. Nature (London) 194: 793-794.

Flamm, D. L. (1977) Analysis of ozone at low concentrations with boric acid buffered KI. Environ. Sci. Technol. 11: 978-983.

Fletcher, B. L.; Tappel, A. L. (1973) Protective effects of dietary alphatocopherol in rats exposed to toxic levels of ozone and nitrogen dioxide. Environ. Res. 6: 165-175.

Folinsbee, L. J.; Bedi, J. F.; Horvath S. M. (1984) Pulmonary function changes in trained athletes following 1-hour continuous heavy exercise while breathing 0.21 ppm ozone. J. Appl. Physiol. Respir. Environ. Exercise Physiol. (In Press).

Folinsbee, L. J.; Drinkwater, B. L.; Bedi, J. F.; Horvath, S. M. (1978) The influence of exercise on the pulmonary changes due to exposure to low concentrations of ozone. In: Folinsbee, L. J.; Wagner, J. A.; Borgia, J. F.; Drinkwater, B. L.; Gliner, J. A.; Bedi, J. F., eds. Environmental stress: individual human adaptations. New York, NY: Academic Press; pp. 125-145.

Fontijn, A.; Sabadell, A. J.; Ronco, R. J. (1970) Homogeneous chemiluminescent measurement of nitric oxide with ozone: Implications for continuous selective monitoring of gaseous air pollutants. Anal. Chem. 42:575-579.

Frager, N. B.; Phalen, R. F.; Kenoyer, J. L. (1979) Adaptations to ozone in reference to mucociliary clearance. Arch. Environ. Health 34: 51-57.

Freeman, B. A.; Mudd, J. B. (1981) Reaction of ozone with sulfhydryls of human erythrocytes. Arch. Biochem. Biophys. 208: 212-220.

Freeman, B. A.; Sharman, M. C.; Mudd, J. B. (1979) Reaction of ozone with phospholipid vesicles and human erythrocyte ghosts. Arch. Biochem. Biophys. 197: 264-272.

Freeman, G.; Juhos, L. T.; Furiosi, N. J.; Mussenden, R.; Stephens, R. J.; Evans, M. J. (1974) Pathology of pulmonary disease from exposure to interdependent ambient gases (nitrogen dioxide and ozone). Arch. Environ. Health 29: 203-210.

Freeman, G.; Stephens, R. J.; Coffin, D. L.; Stara, J. F. (1973) Changes in dog's lungs after long-term exposure to ozone. Arch. Environ. Health 26: 209-216.

Friberg, L.; Holman, B.; Rylander, R. (1972) Animal lung reactions after inhalation of lead and ozone. Environ. Physiol. Biochem. 2: 170-178.

Fried, A.; Hodgeson, J. A. (1982) Laser photoacoustic detection of nitrogen dioxide in the gas-phase titration of nitric oxide and ozone. Anal. Chem. 54: 278-282.

Friedman, M.; Gallo, J. M.; Nichols, H. P.; Bromberg, P. A. (1983) Changes in inert gas rebreathing parameters after ozone exposure in dogs. Am. Rev. Respir. Dis. 128: 851-856.

Fukase, O.; Isomura, K.; Watanabe, H. (1975) Effect of ozone on glutathione in vivo. Taiki Osen Kenkyu 10: 58-62.

Fukase, O.; Watanabe, H.; Isomura, K. (1978) Effects of exercise on mice exposed to ozone. Arch. Environ. Health 33: 198-200.

Gardner, D. E.; Graham, J. A. (1977) Increased pulmonary disease mediated through altered bacterial defenses. In: Sanders, C. L.; Schneider, R. P.; Dagle, G. E.; Ragen, H. A., eds. Pulmonary macrophage and epithelial cells: proceedings of the sixteenth annual Hanford biology symposium; September 1976; Richland, WA. Washington, DC: Energy Research and Development Administration; pp. 1-21. (ERDA symposium series: 43).

Gardner, D. E.; Illing, J. W.; Miller, F. J.; Coffin, D. L. (1974) The effect of ozone on pentobarbital sleeping time in mice. Res. Commun. Chem. Pathol. Pharmacol. 9: 689-700.

Gardner, D. E.; Lewis, T. R.; Alpert, S. M.; Hurst, D. J.; Coffin, D. L. (1972) The role of tolerance in pulmonary defense mechanisms. Arch. Environ. Health 25: 432-438.

Gardner, D. E.; Miller, F. J.; Illing, J. W.; Kirtz, J. M. (1977) Increased infectivity with exposure to ozone and sulfuric acid. Toxicol. Lett. 1: 59-64.

Gardner, D. E.; Pfitzer, E. A.; Christian; R. T.; Coffin, D. L. (1971) Loss of protective factor for alveolar macrophages when exposed to ozone. Arch. Intern. Med. 127: 1078-1084.

Gay, B. W., Jr.; Noonan, R. C.; Bufalini, J. J.; Hanst, P. L. (1976) Photochemical synthesis of peroxyacyl nitrates in gas phase via chlorine - aldehyde reaction. Environ. Sci. Technol. 10: 82-85.

Gay, B. W., Jr.; Bufalini, J. J. (1972a) Photochemical smog and ozone reactions. R. F. Gould, ed., Am. Chem. Soc., Adv. in Chem. Ser. 113: 225.

Gay, B. W., Jr.; Bufalini, J. J. (1972b) Hydrogen peroxide in the urban atmosphere. Environ. Lett. 3: 21-24.

Gershwin, L. J.; Osebold, J. W.; Zee, Y. C. (1981) Immunoglobulin E-containing cells in mouse lung following allergen inhalation and ozone exposure. Int. Arch. Allergy Appl. Immunol. 65: 266-277.

Gertner, A.; Bromberger-Barnea, B.; Dannenberg, A. M., Jr.; Traystman, R.; Menkes, H. (1983a) Responses of the lung periphery to 1.0 ppm ozone. J. Appl. Physiol. Respir. Environ. Exercise Physiol. 55: 770-776.

Gertner, A.; Bromberger-Barnea, B.; Traystman, R.; Menkes, H. (1983c) Effects of ozone in peripheral lung reactivity. J. Appl. Physiol. Respir. Environ. Exercise Physiol. 55: 777-784.

Gertner, A.; Bromberger-Barnea, B.; Traystman, R.; Berzon, D.; Menkes, H. (1983b) Responses of the lung periphery to ozone and histamine. J. Appl. Physiol. Respir. Environ. Exercise Physiol. 54: 640-646.

Gillespie, J. R. (1980) Review of the cardiovascular and pulmonary function studies on beagles exposed for 68 months to auto exhaust and other air pollutants In: Stara, J. F.; Dungworth, D. L.; Orthoefer, J. C.; Tyler, W. S., eds. Long-term effects of air pollutants in canine species. Cincinnati, Ohio: U.S. Environmental Protection Agency; pp. 115-154; EPA 600/8-80-014.

Gliner, J. A.; Horvath, S. M.; Folinsbee, L. J. (1983) Pre-exposure to low ozone concentrations does not diminish the pulmonary function response on exposure to higher ozone concentration. Am. Rev. Respir. Dis. 127: 51-55.

Goldstein, B. D.; Hamburger, S. J.; Falk, G. W.; Amoruso, M. A. (1977) Effect of ozone and nitrogen dioxide on the agglutination of rat alveolar macrophages by concanavalin A. Life Sci. 21: 1637-1644.

Goldstein, B. D.; Lai, L. Y.; Cuzzi-Spada, R. (1974) Potentiation of complement-dependent membrane damage by ozone. Arch. Environ. Health 28: 40-42.

Goldstein, E.; Eagle, M. C.; Hoeprich, P. (1972) Influence of ozone on pulmonary defense mechanisms of silicotic mice. Arch. Environ. Health 24: 444-448.

Goldstein, E.; Tyler, W. S.; Hoeprich, P. D.; Eagle, C. (1971a) Ozone and the antibacterial defense mechanisms of the murine lung. Arch. Intern. Med. 128: 1099-1102.

Goldstein, E.; Tyler, W. S.; Hoeprich, P. D.; Eagle, C. (1971b) Adverse influence of ozone on pulmonary bactericidal activity of murine lungs. Nature (London) 229: 262-263.

Gooch, P. C.; Creasia, D. A.; Brewen, J. G. (1976) The cytogenetic effect of ozone: inhalation and in vitro exposures. Environ. Res. 12: 188-195.

Gordon, T.; Amdur, M. O. (1980) Effects of ozone on respiratory response of guinea pigs to histamine. J. Toxicol. Environ. Health 6: 185-195.

Graham, J. A. (1979) Alteration of hepatic xenobiotic metabolism by ozone. Durham, NC: Duke University. Ph.D. Dissertation.

Graham, J. A.; Menzel, D. B.; Miller, F. J.; Illing, J. W.; Gardner, D. E. (1981) Influence of ozone on pentobarbital-induced sleeping time in mice, rats, and hamsters. Toxicol. Appl. Pharmacol. 61: 64-73.

Graham, J. A.; Menzel, D. B.; Miller, F. J.; Illing, J. W.; Gardner, D. E. (1982a) Effect of ozone on drug-induced sleeping time in mice pretreated with mixed-function oxidase inducers and inhibitors. Toxicol. Appl. Pharmacol. 62: 489-497.

Graham, J. A.; Menzel, D. B.; Miller, F. J.; Illing, J. W.; Ward, R.; Gardner, D.E. (1983a) Influence of ozone on xenobiotic metabolism. In: Lee, S. D.; Mustafa, M. G.; Mehlman, M. A., eds. International symposium on the biomedical effects of ozone and related photochemical oxidants; March 1982; Pinehurst, NC. Princeton, NJ: Princeton Scientific Publishers, Inc.; pp. 95-117. (Advances in modern environmental toxicology: v. 5).

Graham, J. A.; Menzel, D. B.; Mole, M. L.; Miller, F. J.; Gardner, D. E. (1983b) Influence of ozone on pentobarbital pharmacokinetics in mice. Toxicol. Lett. (In Press).

Graham, J. A.; Miller, F. J.; Gardner, D. E.; Ward, R.; Menzel, D. B. (1982b) Influence of ozone and nitrogen dioxide on hepatic microsomal enzymes in mice. J. Toxicol. Environ. Health 9: 849-856.

Grose, E. C.; Gardner, D. E.; Miller, F. J. (1980) Response of ciliated epitheluim to ozone and sulfuric acid. Environ. Res. 22: 377-385.

Grose, E. C.; Richards, J. H.; Illing, J. W.; Miller, F. J.; Davies, D. W.; Graham, J. A.; Gardner, D. E. (1982) Pulmonary host defense responses to inhalation of sulfuric acid and ozone. J. Toxicol. Environ. Health 10: 351-362.

Grosjean, D. (1981) Critical evaluation and comparison of measurement methods for nitrogenous compounds in the atmosphere. Final report, A 706-05 for Coordinating Research Council. Environmental Research and Technology. Westlake Village, CA.

Grosjean, D. (1983) Distribution of atmospheric nitrogenous pollutants at a Los Angeles area smog receptor site. Environ. Sci. Technol. 17: 13-19.

Grosjean, D.; Fung, K.; Collins, J.; Harrison, J.; Breitung, E. (1984) Portable generator for on-site calibration of peroxyacetyl nitrate analyzers. Anal. Chem. 56: 569-573.

Guderian, R. (1977) Air pollution: Phytotoxicity of acidic gases and its significance in air pollution control. In: Ecological studies 22. Chapter 4. Springer-Verlag, Berlin.

Guerrero, R. R.; Rounds, D. E.; Olson, R. S.; Hackney, J. D. (1979) Mutagenic effects of ozone on human cells exposed in vivo and in vitro based on sister chromatid exchange analysis. Environ. Res. 18: 336-346.

Hacskaylo, E. (1973) The Torrey symposium on current aspects of fungal development. IV. Dependence of mycorrhizal fungi on hosts. Bull. Torrey Bot. Club 100: 217-223.

Hadley, J. G.; Gardner, D. E.; Coffin D. L.; Menzel, D. B. (1977) Enhanced binding of autologous cells to the macrophage plasma membrane as a sensitive indicator of pollutant damage. In: Sanders, C. L.; Schneider, R. P.; Dagle G. E.; Ragan, H. A., eds. Pulmonary macrophage and epithelial cells: proceedings of the sixteenth annual Hanford biology symposium; September 1976; Richland, WA. Washington, DC: Energy Research and Development Administration; pp. 1-21. (ERDA symposium series:

Hamelin, C.; Chung, Y. S. (1975) The effect of low concentrations of ozone on Escherichia coli chromosome. Mutat. Res. 28: 131-132.

Hamelin, C.; Chung, Y.S. (1978) Role of the pol, rec, and DNA gene products in the repair of lesions produced in Escherichia coli DNA by ozone. Stud. Biophys. 68: 229-335.

Hamelin, C.; Sarhan, F.; Chung, Y. S. (1977a) Ozone-induced DNA degradation in different DNA polymerase I mutants of E coli K12. Biochem. Biophys. Res. Commun. 77: 220-224.

Hamelin, C.; Sarhan, F.; Chung, Y. S. (1977b) DNA degradation caused by ozone in mucoid mutants of Escherichia coli K12. FEMS Microbiol. Lett. 2: 149-151.

Hammer, D. I.; Hasselblad, V.; Portnoy, B.; Wehrle, P. F. (1974) Los Angeles student nurse study. Daily symptom reporting and photochemical oxidants. Arch. Environ. Health 28: 255-260.

Hanst, P. L.; Gay, B. W.; Spence, J. W. (1981) Atmospheric measurement of trace pollutants. Long path Fourier-transform infrared spectroscopy. Research Triangle Park, NC: U.S. Environmental Protection Agency; EPA report no. EPA-600/3-81-026.

Hanst, P. L.; Wilson, W. E.; Patterson, R. K.; Gay, B. W., Jr.; Chaney, L. W. (1975) A spectroscopic study of California smog. Research Triangle Park, NC. Publication No. EPA-650/4-75-006.

Hanst, P. L.; Wong, N. W.; Bragin, J. (1982) A long-path infrared study of Los Angeles smog. Atmos. Environ. 16: 969-981.

Hauser, T. R.; Kolar, A. M. (1968) Anal. Chem. 40: 231.

Hayes, E. M.; Skelly, J. M. (1977) Transport of ozone from the northeast U.S. into Virginia and its effect on eastern white pines. Plant Dis. Rep. 61: 778-782.

Haylock, J. C.; Rush, J. L. (1976) Studies on the ozone fading of anthraquinone dyes on nylon fibers. Text. Res. J. 46: 1-8.

Haylock, J. C.; Rush, J. L. (1978) Studies on the ozone fading of anthraquinone dyes on nylon fibers. Part II: in-service performance. Text. Res. J. 48: 143-149.

Haynie, F. H.; Spence, J. W.; Upham, J. B. (1976) Effects of gaseous pollutants on materials: a chamber study. Research Triangle Park, NC: U.S. Environmental Protection Agency; EPA Report No. EPA-600/3-76-015.

Hazucha, M.; Silverman, F.; Parent, C.; Field, S.; Bates, D. V. (1973) Pulmonary function in man after short-term exposure to ozone. Arch. Environ. Health 27: 183-188.

Heagle, A. S.; Letchworth, M. B.; Mitchell, C. A. (1983) Injury and yield responses of peanuts to chronic doses of ozone in open-top field chambers. Phytopathology 73: 551-555.

Heagle, A. S.; Philbeck, R. B.; Knott, W. M. (1979a) Thresholds for injury growth, and yield loss caused by ozone or field corn hybrids. Phyptopathology 69: 21-26.

Heagle, A. S.; Spencer, S.; Letchworth, M. B. (1979b) Yield response of winter wheat to chronic doses of ozone. Can. J. Bot., 57: 1999-2005.

Heagle, A. S., and Heck, W. W. (1980) Field methods to assess crop losses due to oxident air pollutants. In: Teng, P. S., and Krupa, A. V., Eds. Crop Loss Assessment: Proceedings of E. C. Stakman Commemorative Symposium. University of Minnesota, Agricultural Experimental Station; Miscellaneous Publications No. 7, Minneaplolis. pp. 296-305

Heagle, A. S., Body, D. E., and Pounds, E. K. (1972) Effect of ozone on yield of sweet corn. Phytopathology 62: 683-687.

Heagle, A. S., Body, D. E., Neely, G. E. (1974) Injury and yield responses of soybean to chronic doses of ozone and sulfur dioxide in the field. Phytopahtology. 64: 132-136.

Heck, W. W. (1973) Air pollution and the future of agriculture. In: Naegele, J. A., ed. Air pollution damage to vegetation. Washington, D.C: American Chemical Society (Advances in Chemistry Series No. 122); pp. 118-129.

Heck, W. W.; Adams, R. M.; Cure, W. W.; Heagle, A. S.; Heggestad, H. E.; Kohut, R. J.; Kress, L. W.; Rawlings, J. O.; Taylor, O. C. (1983) A reassessment of crop loss from ozone. Environ. Sci. Tech., 17: 573A-581A.

Heck, W. W.; Dunning, J. A.; Hindawi, I. J. (1966) Ozone: Non-linear relation of dose and injury in plants. Science 151: 577-578.

Heck, W. W.; Taylor, O. C.; Adams, R.; Bingham, G.; Miller, J.; Preston, E.; Weinstein, L. (1982) Assessment of crop loss from ozone. J. Air. Pollut. Control Assoc., 32: 353-361.

Heck, W. W.; Tingey, D. T. (1971) Ozone time-concentration model to predict acute foliar injury. In: Proceedings of the Second International Clean Air Congress. Englund, H. M.; Beery, W. T.; Eds. Academic Press, New York. pp. 249-255

Heggestad, H. E.; Heagle, A. S.; Bennett, J. H.; Koch, E. J. (1980) The effects of photochemical oxidants on the yield of snap beans. Atmos. Environ. 14: 316-326.

Heikes, B. G.; Lazrus, A. L.; Kok, G. L.; Kunen, S. M.; Gandrud, B. W.; Gitlin, S. N.; Sperry, P. D. (1982) Evidence for aqueous phase hydrogen peroxide synthesis in the troposphere. JGR J. Geophys. Res. 87: 3045-3051.

Henderson, W. R.; Reinert, R. A. (1979) Yield response of four fresh market tomato cultivars after acute ozone exposure in the seedling stage. J. Amer. Soc. Hortic. Sci., 104: 754-759.

Hendry, D. G.; Kenley, R. A. (1977) Generation of peroxy radicals from peroxy nitrates (RO_2NO_2). Decomposition of peroxyacyl nitrates. Atmos. Environ. 99: 3198-3199.

Herman, D. R. (1972) The effect of oxidant air pollution on athletic performance. Chapel Hill, NC: University of North Carolina. Master's Thesis.

Hesterberg, T. W.; Last, J. A. (1981) Ozone-induced acute pulmonary fibrosis in rats. Prevention of increased rates of collagen synthesis by methylprednisolone. Am. Rev. Respir. Dis. 123: 47-52.

Heuss, J. M.; Glasson, W. A. (1968) Hydrocarbon reactivity and eye irritation. Environ. Sci. Technol. 2: 1109-1116.

Hodgeson, J. A.; Hughes, E. E.; Schmidt, W. P.; Bass, A. M. (1977) Methodology for standardization of atmospheric ozone measurements. In: Dimitriades, B., ed. International Conference on Photochemical Oxidant Pollution and Its Control, Vol I. Research Triangle Park, NC: U.S. Environmental Protection Agency; EPA report no. EPA-600/3-77-001a; pp. 3-12.

Hodgeson, J. A.; Krost, K. J.; O'Keeffe, A. E.; Stevens, R. K. (1970) Chemiluminescent measurement of atmospheric ozone. Anal. Chem. 42: 1795-1802.

Hoffman, G. J.; Maas, E. V.; Rawlins, S. L. (1975) Salinity-ozone interactive effects on alfalfa yield and water relations. J. Environ. Qual., 4: 326-331.

Holdren, M. W.; Spicer, C. W. (1984) Field compatible calibration procedure for peroxyacetyl nitrate. Environ. Sci. Technol. 18: 113-116.

Holdren, M. W.; Westberg, H. H.; Zimmerman, P. R. (1979) Analysis of monoterpene hydrocarbons in rural atmospheres. JGR J. Geophys. Res. 84: 5083-5088.

Holtzman, M. I.; Cunningham, J. H.; Sheller, J. R.; Irsigler, G. B.; Nadel, J. A.; Boushey, H. A. (1979) Effect of ozone on bronchial reactivity in atopic and nonatopic subjects. Am. Rev. Respir. Dis. 120: 1059-1067.

Holtzman, M. J.; Fabbri, L. M.; O'Byrne, P. M.; Gold, B. D.; Aizawa, H.; Walters, S. E.; Alpert, S. E.; Nadel, J. A. (1983b) Importance of airway inflammation for hyperresponsiveness induced by ozone. Am. Rev. Respir. Dis. 127: 686-690.

Holtzman, M. J.; Fabbri, L. M.; Skoogh, B.-E.; O'Byrne, P. M.; Walters, E. H.; Aizawa, H.; Nadel, J. A. (1983a) Time course of airway hyperresponsiveness induced by ozone in dogs. J. Appl. Physiol. Respir. Environ. Exercise Physiol. 55: 1232-1236.

Horsman, D. C.; Nocholls, A. O.; Calder, D. M. (1980) Growth responses of Dactylis glomerata, Lolium perenne, and Phalaris aquatica to chronic ozone exposure. Aust. J. Plant Physiol., 7: 511-517.

Horvath, S. M.; Gliner, J. A.; Folinsbee, L. J. (1981) Adaptation to ozone: duration of effect. Am. Rev. Respir. Dis. 123: 496-499.

Horvath, S. M.; Gliner, J. A.; Matsen-Twisdale, J. A. (1979) Pulmonary function and maximum exercise responses following acute ozone exposure. Aviat. Space Environ. Med. 40: 901-905.

Howell, R. K.; Kock, E. J.; and Rose, L. P. (1979) Field assessment of air pollution induced soybean yield losses. Agron. J., 71: 285-288.

Hu, P. C.; Miller, F. J.; Daniels, M. J.; Hatch, G. E.; Graham, J. A.; Gardner, D. E.; Selgrade, M. K. (1982) Protein accumulation in lung lavage fluid following ozone exposure. Environ. Res. 29: 377-388.

Huber, G. L.; Mason, R. J.; LaForce, M.; Spencer, N. J.; Gardner, D. E.; Coffin, D. L. (1971) Alterations in the lung following the administration of ozone. Arch. Intern. Med. 128: 81-87.

Hueter, F. G.; Contner, G. L.; Busch, K. A.; Hinners, R. G. (1966) Biological effects of atmospheres contaminated by auto exhaust. Arch. Environ. Health 12: 553-560.

Huevel, H. M.; Huisman, R.; Schmidt, J. M. (1978) Ozone fading of disperse blue 3 on nylon 6 fibers. In: The influence of physical fiber properties. Text. Res. J. 48: 376-384.

Hunt, W. F.; Curran, T. C. (1982) National and regional trends in ambient ozone measurements, 1975-1981. Research Triangle Park, NC: U.S. Environmental Protection Agency, Office of Air Quality Planning and Standards.

Hurst, D. J.; Coffin, D. L. (1971) Ozone effect on lysosomal hydrolases of alveolar macrophages *in vitro*. Arch. Intern. Med. 127: 1059-1063.

Hurst, D. J.; Gardner, D. E.; Coffin, D. L. (1970) Effect of ozone on acid hydrolases of the pulmonary alveolar macrophage. Res. J. Reticuloendothel. Soc. 8: 288-300.

Hussain, M. Z.; Cross, C. E.; Mustafa, M. G.; Bhatnagar, R. S. (1976b) Hydroxyproline contents and prolyl hydroxylase activities in lungs of rats exposed to low levels of ozone. Life Sci. 18: 897-904.

Hussain, M. Z.; Mustafa, M. G.; Chow, C. K.; Cross, C. E. (1976a) Ozone-induced increase of lung proline hydroxylase activity and hydroxyproline content. Chest 69 (Suppl. 2): 273-275.

Hyde, D.; Orthoefer, J.; Dungworth, D.; Tyler, W.; Carter, R.; Lum, H. (1978) Morphometric and morphologic evaluation of pulmonary lesions in beagle dogs chronically exposed to high ambient levels of air pollutants. Lab. Invest. 38: 455-469.

Ibrahim, A. L.; Zee, Y. C.; Osebold, J. W. (1976) The effects of ozone on the respiratory epithelium and alveolar macrophages of mice. I. Interferon production. Proc. Soc. Exp. Biol. Med. 152: 483-488.

Ibrahim, A. L.; Zee, Y. C.; Osebold, J. W. (1980) The effects of ozone on the respiratory epithelium of mice. II. Ultrastructural alterations. J. Environ. Pathol. Toxicol. 3: 251-258.

Illing, J. W.; Miller, F. J.; Gardner, D. E. (1980) Decreased resistance to infection in exercised mice exposed to NO_2 and O_3. J. Toxicol. Environ. Health 6: 843-851.

Inoue, H.; Sato, S.; Hirose, T.; Kikuchi, Y.; Ubukata, T.; Nagashima, S.; Sasaki, T.; Takishima, T. (1979) A comparative study between functional and pathologic alterations in lungs of rabbits exposed to an ambient level of ozone: functional aspects. Nikkyo Shikkai-Shi 17: 288-296.

Jacobson, J. S. (1977) The effects of photochemical oxidants on vegetation. pp. 163-173 In: Ozone und Begleitsubstanzen im Photochemischen Smog. VDI BER. (270).

Japar, S. M.; Niki, H. (1975) Gas-phase reactions of the nitrate radical with olefins. J. Phys. Chem. 79: 1629-1632.

Jayanty, R. K. M.; Blackard, A.; McElroy, F. F.; McClenny, W. A. (1982) Laboratory evaluation of nonmethane organic carbon determination in ambient air by cryogenic preconcentration and flame ionization detection. Research Triangle Park, NC: U.S. Environmental Protection Agency; EPA report no. EPA-600/4-82-019.

Jegier, Z. (1973) Ozone as an air pollutant. Can. J. Public Health 64: 161-166.

Johnson, A. H.; Siccama, T. G. (1983) Acid deposition and forest decline. Environ. Sci. Technol. 17: 294A-305A.

Johnson, D. F.; Kok, G. L.; Sonner, R. J. (1981) Improved chromotropic acid technique for the determination of formaldehyde. In: Grosjean, D; Kok, G. L., eds. Interlaboratory comparison study of methods for measuring formaldehyde and other aldehydes in ambient air. Final report prepared for Coordinating Research Council, Atlanta, GA.

Jorgen, R. T.; Meyer, R. A.; Hughes, R. A. (1978) Routine peroxyacetyl nitrate (PAN) monitoring applied to the Houston Area Oxidant Study. Presented at 71st Annual Meeting of the Air Pollution Control Association; June; Houston, TX. Paper No. 78-50.1.

Joshi, S. B.; Bufalini, J. J. (1978) Halocarbon interferences in chemiluminescent measurements of NO_x. Environ. Sci. Technol. 12:597-599.

Kagawa, J. (1983) Effects of ozone and other pollutants on pulmonary function in man. In: Lee, S. D.; Mustafa, M. G.; Mehlman, M. A., eds. International symposium on the biomedical effects of ozone and related photochemical oxidants; March 1982; Pinehurst, NC. Princeton, NJ: Princeton Scientific Publishers, Inc.; pp. 411-422. (Advances in modern toxicology: v .5).

Kagawa, J.; Toyama, T. (1975) Photochemical air pollution: its effects on respiratory function of elementary school children. Arch. Environ. Health 30: 117-122.

Kagawa, J.; Toyama, T.; Nakaza, M. (1976) Pulmonary function test in children exposed to air pollution. In: Finkel, A. J.; Duel, W. C., eds. Clinical implications of air pollution research: proceedings of the 1974 air pollution medical research conference; December 1974; San Francisco, CA. Acton, MA: Publishing Sciences Group, Inc.; pp. 305-320.

Kamath, Y. K.; Ruetsch, S. B.; Weigmann, H. D. (1982) Micro-spectrophotometric study of ozone fading of disperse dyes in nylon. Text. Res. J.: in press.

Kavlock, R. J.; Meyer, E.; Grabowski, C. T. (1980) Studies on the developmental toxicity of ozone: postnatal effects. Toxicol. Lett. 5: 3-9.

Kavlock, R.; Daston, G.; Grabowski, C. T. (1979) Studies on the developmental toxicity of ozone. I. Prenatal effects. Toxicol. Appl. Pharmacol. 48: 19-28.

Kehrl, H. R.; Hazucha, M. J.; Solic, J.; Bromberg, P. A. (1983) Effects of ozone exposure on humans with moderate irreversible chronic obstructive lung disease. In: Mehlman, M. A.; Lee, S. D.; Mustafa, M. G., eds. International symposium on the biomedical effects of ozone and related photochemical oxidants; March 1982; Pinehurst, NC. Princeton, NJ: Princeton Scientific Publishers, Inc.; pp. 213-225. (Advances in modern environmental toxicology: v. 5.)

Kelly, T. V.; Stedman, D. H.; Kok, G. L. (1979) Measurements of H_2O_2 and HNO_3 in rural air. Geophys. Res. Lett. 6: 375-378.

Kenoyer, J. L.; Phalen, R. F.; Davis, J. R. (1981) Particle clearance from the respiratory tract as a test of toxicity: effect of ozone on short and long term clearance. Exp. Lung Respir. 2: 111-120.

Kerr, N.; Morris, M. A.; Zeronian, S. H. (1969) The effect of ozone and laundering on a vat-dyed cotton fabric. Am. Dyest. Rep. 58: 34-36.

Kesner, L.; Kindya, R. J.; Chan, P. C. (1979) Inhibition of erythrocyte membrane (Na^++K^+)-activated ATPase by ozone-treated phospholipids. J. Biol. Chem. 254: 2705-2709.

Kindya, R. J.; Chan, P. C. (1976) Effect of ozone on erythrocyte membrane adenosine triphosphatase. Biochim. Biophys. Acta 429: 608-615.

Kohut, R.; Laurence, J. A. (1983) Yield response of red kidney bean to incremental ozone concentrations in field. Environ. Pollut. (Ser A), 32: 233-240.

Kok, G. L.; Darnall, K. R.; Winer, A. M.; Pitts, J. N., Jr.; Gay, B. W., Jr. (1978a) Ambient air measurements of hydrogen peroxide in the California South Coast Air Basin. Environ. Sci. Technol. 12: 1077-1080.

Kok, G. L.; Holler, T. P.; Lopez, M. B.; Nachtrieb, H. A.; Yuan, M. (1978b) Chemiluminescent method for determination of hydrogen peroxide in the ambient atmosphere. Environ. Sci. Technol. 12: 1072-1076.

König, G.; Rommelt, H.; Kienele, H.; Dirnagl, K.; Polke, H.; Fruhmann, G. (1980) Changes in the bronchial reactivity of humans caused by the influence of ozone. Arbeitsmed. Sozialmed. Praeventivmed. 151: 261-263.

Konigsberg, A. S.; Bachman, C. H. (1970) Ozonized atmosphere and gross motor activity of rats. Int. J. Biometeorol. 14: 261-266.

Koontz, A. E.; Heath, R. L. (1979) Ozone alteration of transport of cations and the Na^+/K^+ ATPase in human erythrocytes. Arch. Biochem. Biophys. 198: 493-500.

Kravetz, T. M.; Martin, S. W.; Mendenhall, G. D. (1980) Synthesis of peroxyacetyl and peroxyaroyl nitrates. Complexion of peroxyacetyl nitrate with benzene. Environ. Sci. Technol. 14: 1262-1264.

Kress, L. W.; Miller, J. E. (1983) Impact of ozone on soybean yield. J. Environ. Qual., 12: 276-281.

Kress, L. W.; Skelly, J. M. (1982) Response to several eastern forest tree species to chronic doses of ozone and nitrogen dioxide. Plant Dis. Rep., 66: 1149-1152.

Kulle, T. J.; Milman, J. H.; Sauder, L. R.; Kerr, H. D.; Farrell, B. P.; Miller, W. R. (1984) Pulmonary function adaptation to ozone in subjects with chronic bronchitis. Environ. Res. (In Press).

Kulle, T. J.; Sauder, L. R.; Kerr, H. D.; Farrell, B. P.; Bermel, M. S.; Smith, D. M. (1982) Duration of pulmonary function adaptation to ozone in humans. Am. Ind. Hyg. Assoc. J. 43: 832-837.

Kuntz, R.; Lonneman, W.; Namie, G.; Hull, L. A. (1980) Rapid determination of aldehydes in air analyses. Anal. Lett. 13:1409-1415.

Kyei-Aboagye, K.; Hazucha, M.; Wyszogrodski, I.; Rubinstein, D.; Avery, M. E. (1973) The effect of ozone exposure in vivo on the appearance of lung tissue lipids in the endobronchial lavage of rabbits. Biochem. Biophys. Res. Commun. 54: 907-913.

Larkin, E.C.; Goheen, S.C.; Rao, G.A. (1983) Morphology and fatty acid composition of erythrocytes from monkeys exposed to ozone for one year. Environ. Res. 32: 445-454.

Last, J. A.; Cross, C. E. (1978) A new model for health effects of air pollutants: evidence for synergistic effects of mixtures of ozone and sulfuric acid aerosols on rat lungs. J. Lab. Clin. Med. 91: 328-339.

Last, J. A.; Dasgupta, P. K.; DeCesare, K.; Tarkington, B.K. (1982) Inhalation toxicology of ammonium persulfate, an oxidant aerosol, in rats. Toxicol. Appl. Pharmacol. 63: 257-263.

Last, J. A.; Greenberg, D. B. (1980) Ozone-induced alterations in collagen metabolism of rat lungs. II. Long-term exposure. Toxicol. Appl. Pharmacol. 55: 108-114.

Last, J. A.; Greenberg, D. B.; Castleman, W. L. (1979) Ozone-induced alterations in collagen metabolism of rat lungs. Toxicol. Appl. Pharmacol. 51: 247-258.

Last, J. A.; Jennings, M. D.; Schwartz, L. W.; Cross, C. E. (1977) Glycoprotein secretion by tracheal explants cultured from rats exposed to ozone. Am. Rev. Respir. Dis. 116: 695-703.

Last, J. A.; Kaizu, T. (1980) Mucus glycoprotein secretion by tracheal explants: effects of pollutants. EHP Environ. Health Perspect. 35: 131-138.

Lebowitz, M. D. (1984) The effects of environmental tobacco smoke exposure and gas stoves on daily peak flow rates in asthmatic and non-asthmatic families. Eur. J. Respir. Dis. 65 (suppl. 133): 90-97.

Lebowitz, M. D.; Bendheim, P.; Cristea, G.; Markowitz, D.; Misiaszek, Jr.; Staniec, M.; Van Wyck, D. (1974) The effect of air pollution and weather on lung function in exercising children and adolescents. Am. Rev. Respir. Dis. 109: 262-273.

Lebowitz, M. D.; Holberg, C. J.; Dodge, R. R. (1983) Respiratory effects on populations from low level exposures to ozone. Presented at: 34th annual meeting of the Air Pollution Control Association; June; Atlanta, GA. Pittsburgh, PA: Air Pollution Control Association; paper no. 83-12.5.

Lebowitz, M. D.; O'Rourke, M. K.; Dodge, R.; Holberg, C. J.; Corman, G.; Hoshaw, R. W.; Pinnas, J. L.; Barbee, R. A.; Sneller, M. R. (1982) The adverse health effects of biological aerosols, other aerosols, and indoor microclimate on asthmatics and nonasthmatics. Environ. Int. 8: 375-380.

Lee, L.-Y.; Bleecker, E. R.; Nadel, J. A. (1977) Effect of ozone on bronchomotor response to inhaled histamine aerosol in dogs. J. Appl. Physiol. Respir. Environ. Exercise Physiol. 43: 626-631.

Lewis, T. E.; Brennan, E.; Lonneman, W. A. (1983) PAN concentrations in ambient air in New Jersey. J. Air Pollut. Control Assoc. 33: 885-887.

Lewis, T. R.; Hueter, F. G.; Busch, K. A. (1967) Irradiated automobile exhaust: its effects on the reproduction of mice. Arch. Environ. Health 15: 26-35.

Lewis, T. R.; Moorman, W. J.; Yang, Y.; Stara, J. F. (1974) Long-term exposure to auto exhaust and other pollutant mixtures. Effects on pulmonary function in the beagle. Arch. Environ. Health 29: 102-106.

Linn, W. S.; Avol, E. L.; Hackney, J. D. (1983) Effects of ambient oxidant pollutants on humans: a movable environmental chamber study. In: Lee, S. D.; Mustafa, M. G.; Mehlman, M. A., eds. International symposium on the biomedical effects of ozone and related photochemical oxidants; March 1982; Pinehurst, NC. Princeton, NJ: Princeton Scientific Publishers, Inc.; pp. 125-137. (Advances in modern toxicology: v. 5).

Linn, W. S.; Buckley, R. D.; Spier, C. E.; Blessey, R. L.; Jones, M. P.; Fischer, D. A.; Hackney, J. D. (1978) Health effects of ozone exposure in asthmatics. Am. Rev. Respir. Dis. 117: 835-843.

Linn, W. S.; Fischer, D. A.; Medway, D. A.; Anzar, U. T.; Spier, C. E.; Valencia, L. M.; Venct, T. G.; Hackney, J. D. (1982a) Short-term respiratory effects of 0.12 ppm ozone exposure in volunteers with chronic obstructive lung disease. Am. Rev. Respir. Dis. 125: 658-663.

Linn, W. S.; Jones, M. P.; Bachmayer, E. A.; Spier, C. E.; Mazur, S. F.; Avol, E. L.; Hackney, J. D. (1980) Short-term respiratory effects of polluted ambient air: a laboratory study of volunteers in a high-oxidant community. Am. Rev. Respir. Dis. 121: 243-252.

Linn, W. S.; Medway, D. A.; Anzar, U. T.; Valencia, L. M.; Spier, C. E.; Tsao, F. S-O.; Fischer, D. A.; Hackney, J. D. (1982b) Persistence of adaptation to ozone in volunteers exposed repeatedly over six weeks. Am. Rev. Respir. Dis. 125: 491-495.

Linn, W. S.; Shamoo, D. A.; Venet, T. G.; Spier, C. E.; Valencia, L. M.; Anzar, U. T.; Hackney, J. D. (1983) Response to ozone in volunteers with chronic obstructive pulmonary disease. Arch. Environ. Health 38: 278-283.

Lipari, F.; Swarin, S. (1982) Determination of formaldehyde and other aldehydes in automobile exhaust with an improved 2,4-dinitrophenylhydrazine method. J. Chromatogr. 247:297-306.

Logan, J. A. (1983) Nitrogen oxides in the troposphere: global and regional budgets. JGR J. Geophys. Res. 88: 10785-10807.

Logan, J. A.; Prather, M. J.; Wofsy, S. C.; McElroy, M. B. (1981) Tropospheric chemistry: a global perspective. JGR J. Geophys. Res. 86: 7210-7254.

Lonneman, W. A.; Bufalini, J. J.; Namie, G. R. (1982) Calibration procedure for PAN based on its thermal decomposition in the presence of nitric oxide. Environ. Sci. Technol. 16: 655-660.

Lonneman, W. A.; Bufalini, J. J.; Seila, R. L. (1976) PAN and oxidant measurement in ambient atmospheres. Environ. Sci. Technol. 10: 274-280.

Luck, R. F. (1980) Impact of oxidant air pollution on ponderosa and Jeffrey pine cone production. In: Miller, P.R., ed. Proceedings of the symposium on the effects of air pollutants on Mediterranean and temperate forest ecosystems; June; Riverside, CA. Berkeley, CA: U.S. Department of Agriculture, Forest Service; genl. tech. report no. PSW-43; p. 256.

Lum, H.; Schwartz, L. W.; Dungworth, D. L.; Tyler, W. S. (1978) A comparative study of cell renewal after exposure to ozone or oxygen. Response of terminal bronchiolar epithelium in the rat. Am. Rev. Respir. Dis. 118: 335-345.

Lunan, K. D.; Short, P.; Negi, D.; Stephens, R. L. (1977) Glucose-6-phosphate dehydrogenase response of postnatal lungs to NO$_2$ and O$_3$. In: Sanders, C. L.; Schneider, R. P.; Dagle, G. E.; Ragan, H. A., eds. Pulmonary macrophage and epithelial cells: proceedings of the sixteenth annual Hanford biology symposium; September 1976; Richland, WA. Washington, DC: Energy Research and Development Administration; pp. 236-247. (ERDA symposium series: 43).

MacLean, D. C.; Schneider, P. E. (1976) Photochemcial oxidants in Yonkers, New York. J. Environ. Qual., 5: 75-78.

MacRae, W. D.; Stich, H. F. (1979) Induction of sister chromatid exchanges in Chinese hamster ovary cells by Thiol and hydrazene compounds. Mutat. Res. 68: 351-365.

Makino, K.; Mizoguchi, I. (1975) Symptoms caused by photochemical smog. Nippon Koshu Eisei Zasshi 22: 421-430.

Male, L.; Preston, E.; Neely, G. (1983) Yield response curves of crops exposed to SO$_2$. Atmos. Environ., 17: 1589-1593.

Manion, P. (1981) Tree disease concepts. Englewood Cliffs, NJ: Prentice-Hall, Inc.; pp. 12-16, 325-339.

Mann, L. K.; McLaughlin, S. B.; Shriner, D. S. (1980) Seasonal physiological responses of white pine under chronic air pollution stress. Environ. Exp. Bot., 20: 99-105.

Martin, C. J.; Boatman, E. S.; Ward, G. (1983) Mechanical properties of alveolar wall after pneumonectomy and ozone exposure. J. Appl. Physiol. Respir. Environ. Exercise Physiol. 54: 785-788.

Martinez, J. R.; Singh, H. B. (1979) Survey of the role of NO_x in nonurban ozone formation. Prepared by SRI International for U.S. Environmental Protection Agency, Research Triangle Park, NC. EPA report no. EPA-450/4-79-035.

Mast, G. M.; Saunders, H. E. (1962) Research and development of the instrumentation of ozone sensing. ISA Trans. 1: 325-328.

Mayrsohn, H.; Brooks, C. (1965) The analysis of PAN by electron capture gas chromatography. Presented at the Western Regional Meeting of the American Chemical Society, Los Angeles, CA.

McAllen, S. J.; Chiu, S. P.; Phalen, R. F.; Rasmussen, R. E. (1981) Effect of *in vivo* ozone exposure on *in vitro* pulmonary alveolar macrophage mobility. J. Toxicol. Environ. Health 7: 373-381.

McBride, J. M.; McClenny, W. A. (1980) Analysis of NMOC by cryogenic preconcentration and flame ionization detection. Draft Report. U. S. Environmental Protection Agency, Research Triangle Park, NC.

McCarthy, E. F.; Stankunas, A. R.; Yocum, J. E.; Rae, D. (1983) Damage cost models for pollutant effects on material. East Hartford, CT: TRC Environmental Consultants, Inc.; TRC project no. 1574-J80. U.S. Environmental Protection Agency; EPA report no. 600/3-84-012.

McDonnell, W. F.; Horstmann, D. H.; Hazucha, M. J.; Seal, E., Jr.; Haak, E. D.; Salaam, S.; House, D. E. (1983) Pulmonary effects of ozone exposure during exercise: dose-response characteristics. J. Appl. Physiol. Respir. Environ. Exercise Physiol. 54: 1345-1352.

McElroy, F. F. (1979) Transfer standards for calibration of ambient air monitoring analyzers for ozone: technical assistance document. Research Triangle Park, NC. U.S. Environmental Protection Agency; EPA report no. EPA-600/4-79-056.

McElroy, F. F.; Thompson, V. L. (1975) Hydrocarbon measurement discrepancies among various analyzers using flame-ionization detectors. Research Triangle Park, NC: U.S. Environmental Protection Agency; EPA report no. EPA-600/4-75-010.

McJilton, C.; Thielke, J.; Frank, R. (1972) Ozone uptake model for the respiratory system. In: Abstracts of technical papers: American industrial hygiene conference; May 1972; San Francisco, CA. Am. Ind. Hyg. Assoc. J. 33(2): paper no. 45.

McLaughlin, S. B.; McConathy, R. K.; Duvick, D.; Mann, L. K. (1982) Effects of chronic air pollution stress on photosynthesis, carbon allocation and growth of white pine trees. For. Sci. 28: 60-70.

McLaughlin, S. B.; Shriner, D. S.; McConathy, R. K.; Mann, L. K. (1979) The effects of SO_2 dosage kinetics and exposure frequency on photosynthesis and transpiration of kidney beans (*Phaseolus vulgaris* L.). Environ. Exp. Bot., 19: 179-191.

McMillan, R. S.; Wiseman, D. H.; Hanes, B.; Wehrle, P. F. (1969) Effect of oxidant air pollution on peak expiratory flow rates in Los Angeles school children. Arch. Environ. Health 18: 94-99.

Mellick, P. W.; Dungworth, D. L.; Schwartz, L. W.; Tyler, W. S. (1977) Short-term morphologic effects of high ambient levels of ozone on lungs of rhesus monkeys. Lab. Invest. 36: 82-90.

Mellick, P. W.; Mustafa, M. G.; Tyler, W. S.; Dungworth, D. L. (1975) Morphologic and biochemical changes in primate lung due to low-level ozone exposure. Bull. Int. Union Against Tuberculosis 51: 565-567.

Meloan, C. E.; Mauck, M.; Huffman, C. (1961) Spectrophotometric determination of traces of hydrogen peroxide. Anal. Chem. 33: 104-106.

Menzel, D. B.; Roehm, J. N.; Lee, S. D. (1972) Vitamin E: the biological and environmental antioxidant. J. Agric. Food Chem. 20: 481-486.

Menzel, D. B.; Slaughter, R. J.; Bryant, A. M.; Jauregui, H. O. (1975a) Heinz bodies formed in erythrocytes by fatty acid ozonides and ozone. Arch. Environ. Health 30: 296-301.

Menzel, D. B.; Slaughter, R. J.; Bryant, A. M.; Jauregui, H. O. (1975b) Prevention of ozonide-induced Heinz bodies in human erythrocytes by vitamin E. Arch. Environ. Health 30: 234-236.

Meyer, D. A.; Sommer, J. G. (1957) Final technical report: the development of weather and aging resistant pneumatic tires and mechanical rubber goods. Dayton, OH: Dayton Rubber Co.

Miller, F. J.; Illing, J. W.; Gardner, D. E. (1978) Effect of urban ozone levels on laboratory-induced respiratory infections. Toxicol. Lett. 2: 163-169.

Miller, F. J.; McNeal, C. A.; Kirtz, J. M.; Gardner, D. E.; Coffin, D. L.; Menzel, D. B. (1979) Nasopharyngeal removal of ozone in rabbits and guinea pigs. Toxicology 14: 273-281.

Miller, P. R. (1973) Oxidant-induced community change in a mixed conifer forest. In: Naegele, J.A., ed. Air pollution damage to vegetation. Washington, DC: American Chemical Society, (Advances in chemistry series: no. 122); pp. 101-117.

Miller, P. R.; Elderman, M. J., eds. (1977) Photochemical oxidant air pollutant effects on a mixed conifer forest ecosystem: a progress report, 1976. Corvallis, OR: U.S. Environmental Protection Agency; EPA report no. EPA-600/3-77-104. Available from: NTIS, Springfield, VA; PB-274531.

Miller, P. R.; Parmeter, J. R., Jr.; Taylor, O. C.; Cardiff, E. A. (1963) Ozone injury to the foliage of Pinus ponderosa. Phytopathology 53: 1072-1076.

Miller, P. R.; Taylor, O. C.; Wilhour, R. G. (1982) Oxidant air pollution effects on a western coniferous forest ecosystem. EPA-600/D-82-276. U.S. Environmental Protection Agency, Corvallis, Oregon.

Miller, P. R.; Taylor, O. C.; Wilhour, R. G. (1982) Oxidant air pollution effects on a western coniferous forest ecosystem. Corvallis, OR: U.S. Environmental Protection Agency; EPA-600/D-82/276; 10 pp.

Mizoguchi, I.; Osawa, M.; Sato, Y.; Makino, K.; Yagyu, H. (1973) Studies on erythrocyte and photochemical smog. I. Effects of air pollutants on erythrocyte resistance. Taiki Osen Kenkyu 8: 414.

Moore, G. S.; Calabrese, E. J.; Grinberg-Funes, R. A. (1980) The C57L/J mouse strain as a model for extrapulmonary effects of ozone exposure. Bull. Environ. Contam. Toxicol. 25: 578-585.

Moore, G. S.; Calabrese, E. J.; Labato, F. J. (1981a) Erythrocyte survival in sheep exposed to ozone. Bull. Environ. Contam. Toxicol. 27: 126-138.

Moore, G. S.; Calabrese, E. J.; Schulz, E. (1981b) Effect of in vivo ozone exposure to dorset sheep, an animal model with low levels of erythrocyte glucose-6-phosphate dehydrogenase activity. Bull. Environ. Contam. Toxicol. 26: 273-280.

Moore, P. F.; Schwartz, L. W. (1981) Morphological effects of prolonged exposure to ozone and sulfuric acid aerosol on the rat lung. Exp. Mol. Pathol. 35: 108-123.

Moorman, W. J.; Chmiel, J. J.; Stara, J. F.; Lewis, T. R. (1973) Comparative decomposition of ozone in the nasopharynx of beagles. Acute vs. chronic exposure. Arch. Environ. Health 26: 153-155.

Mottola, H. A.; Simpson, B. E.; Gorin, G. (1970) Absorptiometric determination of hydrogen peroxide in submicrogram amounts with leuco crystal violet and peroxidase as catalyst. Anal. Chem. 42: 410-411.

Mueller, P. K.; Hidy, G. M. (1983) The sulfate regional experiment (SURE): report of findings. Palo Alto, CA: Electric Power Research Institute; report no. EA-1901.

Mueller, W. J.; Stickney, P. B. (1970) A survey and economic assessment of the effects of air pollution on elastomers. Columbus, OH: Battelle Memorial Institute; NAPCA contract no. CPA-22-69-146.

Murphy, S. D. (1964) A review of effects on animals of exposure to auto exhaust and some of its components. J. Air Pollut. Control Assoc. 14: 303-308.

Murphy, S. D.; Leng, J. K.; Ulrich, C. E.; Davis, H. V. (1963) Effects on animals of exposure to auto exhaust. Arch. Environ. Health 7: 60-70.

Murphy, S. D.; Ulrich, C. E.; Frankowitz, S. H.; Xintaras, C. (1964) Altered function in animals inhaling low concentrations of ozone and nitrogen dioxide. Am. Ind. Hyg. Assoc. J. 25: 246-253.

Musselman, R. C.; Oshima, R. J.; Gallavan, R. E. (1983) Significance of pollutant concentration distribution on the response of red kidney beans to ozone. J. Amer. Soc. Hort. Sci., 108: 347-351.

Mustafa, M. G. (1975) Influence of dietary vitamin E on lung cellular sensitivity to ozone in rats. Nutr. Rep. Int. 11: 473-476.

Mustafa, M. G.; DeLucia, A. J.; York, G. K.; Arth, C.; Cross, C. E. (1973) Ozone interaction with rodent lung. II. Effects on oxygen consumption of mitochondria. J. Lab. Clin. Med. 82: 357-365.

Mustafa, M. G.; Elsayed, N. M.; Quinn, C. L.; Postlethwait, E. M.; Gardner, D. E.; Graham, J. A. (1982) Comparison of pulmonary biochemical effects of low level ozone exposure on mice and rats. J. Toxicol. Environ. Health 9: 857-865.

Mustafa, M. G.; Hacker, A. D.; Ospital, J. J.; Hussain, M. Z.; Lee, S.D. (1977) Biochemical effects of environmental oxidants pollutants in animal lungs. In: Lee, S.D., ed. Biochemical effects of environmental pollutants. Ann Arbor, MI: Ann Arbor Science Publishers, Inc.; pp. 59-96.

Mustafa, M. G.; Lee, S. D. (1976) Pulmonary biochemical alterations resulting from ozone exposure. Ann. Occup. Hyg. 19: 17-26.

Mustafa, M. G.; Tierney, D. F. (1978) Biochemical and metabolic changes in the lung with oxygen, ozone, and nitrogen dioxide toxicity. Am. Rev. Respir. Dis. 118: 1061-1090.

Nakajima, T.; Kusumoto, S.; Tsubota, Y.; Yonekawa, E.; Yoshida, R.; Motomiya, K.; Ito, K.; Ide, G.; Ostu, H. (1972). Histopathological changes in the respiratory organs of mice exposed to photochemical oxidants and automobile exhaust gas. Osaka-Furitsu Koshu Eisei Kenkyusho Kenkyu Hokoku Rodo Eisei Hen 10: 35-42.

National Academy of Sciences, National Research Council. (1977) Ozone and other photochemical oxidants. Washington, DC: National Academy Press; pp. 45-125 and chapters 4 and 6.

Nederbragt, G. W.; Van der Horst, A.; Van Duijn, J. (1965) Rapid ozone determination near an accelerator. Nature (London) 206: 87.

Neely, G. E.; Tingey, D. T.; Wilhour, R. G. (1977) Effects of ozone and sulfur dioxide singly and in combination on yield, quality, and N-fixation of alfalfa. pp. 663-673 In: International Conference on Photochemical Oxidant Pollution and its Control. Proceedings. Volumn II. B. Dimitriades, ed. EPA-600/3-77-001b. U.S. Environmental Protection Agency, Research Triangle Park, N.C.

Newman, J. R. (1979) Effects of industrial air pollution on wildlife. Biol. Conserv. 15: 181-190.

Nicksic, S. W.; Harkins, J.; Mueller, P. K. (1967) Some analyses for PAN and studies of its structure. Atmos. Environ. 1: 11-18.

Nielsen, T.; Hansen, A. M.; Thomsen, E. L. (1982) A convenient method for preparation of pure standards of peroxyacetyl nitrate for atmospheric analysis. Atmos. Environ. 16: 2447-2450.

Niki, H.; Maker, P. D.; Savage, C. M.; Breitenbach, L. P. (1983) Atmospheric ozone-olefin reactions. Environ. Sci. Technol. 17: 312A-322A.

Nipe, M. R. (1981) Atmospheric contaminant fading. Text. Chem. Color. 13(6): 18-28.

Odum, E. P. (1971) Fundamentals of ecology, third edition. Philadelphia, PA: W. B. Saunders; pp. 1-38.

Ogata, G.; Mass, E. V. (1973) Interactive effects of salinity and ozone on growth and yield of garden beet. J. Environ. Qual., 2: 518-520.

Ogle, L. D.; Hall, R. C.; Crow, W. L.; Jones, A. E. (1982) Development of preconcentration and chromatographic procedures for the continuous and unattended monitoring of hydrocarbons in ambient air. Presented at the 184th National Meeting of the American Chemical Society; September; Kansas City, MO.

Okawada, N.; Mizoguchi, I.; Ishiguro, T. (1979) Effects of photochemical air pollution on the human eye--concerning eye irritation, tear lysome and tear pH. Nagoya J. Med. Sci. 41: 9-20.

Ormrod, D. P. (1982) Air pollutant interactions in mixtures. In: Effects of Air Pollution in Agriculture and Horticulture. Unsworth, M. H.; Ormrod, D. P., eds. Butterworths, London. pp. 307-331.

Osebold, J. W.; Gershwin, L. J.; Zee, Y. C. (1980) Studies on the enhancement of allergic lung sensitization by inhalation of ozone and sulfuric acid aerosol. J. Environ. Pathol. Toxicol. 3: 221-234.

Osebold, J. W.; Owens, S. L.; Zee, Y. C.; Dotson, W. M.; Labarre, D. D. (1979) Immunological alterations in the lungs of mice following ozone exposure: changes in immunoglobulin levels and antibody-containing cells. Arch. Environ. Health 34: 258-265.

Oshima, R. J. (1973) Effects of ozone on a commercial sweet corn variety. Plant Dis. Resp., 57: 719-723.

Oshima, R. J.; Braegelmann, P. K.; Flagler, R. B.; Teso, R. R. (1979) The effects of ozone on the growth, yield, and partitioning of dry matter in cotton. J. Environ. Qual., 8: 474-479.

Oshima, R. J.; Taylor, O. C.; Braegelmann, P. K.; Baldwin, D. W. (1975) Effects of ozone on the yield and plant biomass of a commercial variety of tomato. J. Environ. Qual., 4: 463-464.

Oshima, R.; Taylor, O. C.; Cardiff, E. A. (1974) Severe air pollution episode in South Coast Basin. Calif. Agric. 28: 12-13.

Osman, M.; Hill, H. H.; Holdren, M. W.; Westberg, H. H. (1979) Vapor-phase silylation of alcohols for air analysis. In: A. Zlatkis, ed. Advances in Chromatography, Chromatography Symposium-University of Houston, Houston, TX.

P'an, A. Y. S.; Beland, J.; Jegier, Z. (1972) Ozone-induced arterial lesions. Arch. Environ. Health 24: 229-232.

P'an, A. Y. S.; Jegier, Z. (1971) The serum trypsin inhibitor capacity during ozone exposure. Arch. Environ. Health 23: 215-219.

P'an, A. Y. S.; Jegier, Z. (1972) Trypsin protein esterase in relation to ozone-induced vascular damage. Arch. Environ. Health 24: 233-236.

P'an, A. Y. S.; Jegier, Z. (1976) Serum protein changes during exposure to ozone. Am. Ind. Hyg. Assoc. J. 37: 329-334.

Parmeter, J. R., Jr.; Bega, R. V.; Neff, T. (1962) A chlorotic decline of ponderosa pine in southern California. Plant Dis. Rep. 46: 269-273.

Pate, C. T.; Atkinson, R.; Pitts, J. N., Jr. (1976) The gas phase reaction of O_3 with a series of aromatic hydrocarbons. J. Environ. Sci. Health A11: 1-10.

Patton, R. L. (1981) Effects of ozone and sulfur dioxide on height and stem specific gravity of Populus Hybrids. For. Sci. Res. Paper NE-471.

Paur, R. J.; Bass, A. M. (1983) Standard reference photometer for the assay of ozone. Presented at the National Meeting of the American Chemical Society; October; Washington, DC.

Paur, R. J.; McElroy, F. F. (1979) Technical assistance document for calibration of ambient ozone monitors. Research Triangle Park, NC: U.S. Environmental Protection Agency; EPA report no. EPA-600/4-79-057.

Peake, E.; Sandhu, H. S. (1982) The formation of ozone and peroxyacetyl nitrate (PAN) in the urban atmospheres of Alberta. Presented at 65th Annual Conference Chem. Inst. Canada; May 30 - June 2,1982; Toronto, Canada.

Pell, E. J.; Weissberger, W. C.; Speroni, J. J. (1980) Impact of ozone on quantity and quality of greenhouse-grown potato plants. Environ. Sci. Technol., 14: 568-571.

Perschke, H.; Broda, E. (1961) Determination of very small amounts of hydrogen peroxide. Nature (London) 190: 257-258.

Peterson, D. C.; Andrews, H. L. (1963) The role of ozone in radiation avoidance in the mouse. Radiat. Res. 19: 331-336.

Phalen, R. F.; Kenoyer, J. L.; Crocker, T. T.; McClure, T. R. (1980) Effects of sulfate aerosols in combination with ozone on elimination of tracer particles inhaled by rats. J. Toxicol. Environ. Health 6: 797-810.

Pilz, W.; Johann, I. (1974) Measurement of very small quantities of hydrogen peroxide in air. Int. J. Environ. Anal. Chem. 3: 257-270.

Pisarevskii, A. M.; Polozova, I. P. (1980) Electrode for potentiometric determinations of hydrogen peroxide in alkaline media. Zh. Anal. Khim. 35: 2187-2194.

Plopper, C. G.; Chow, C. K.; Dungworth, D. L.; Brummer, M.; Nemeth, T. J. (1978) Effect of low level of ozone on rat lungs. II. Morphological responses during recovery and reexposure. Exp. Mol. Pathol. 29: 400-411.

Plopper, C. G.; Chow, C. K.; Dungworth, D. L.; Tyler, W. S. (1979) Pulmonary alterations in rats exposed to 0.2 and 0.1 ppm ozone: a correlated morphological and biochemical study. Arch. Environ. Health 34: 390-395.

Pobiner, H. (1961) Determination of hydroperoxides in hydrocarbons by conversion to hydrogen peroxide and measurement by titanium complexing. Anal. Chem. 33: 1423-1426.

Pratt, G. C. (1982) Effects of ozone and sulfur dioxide on soybeans. PhD Thesis. University of Minnesota, Minneapolis.

Raub, J. A.; Miller, F. J.; Graham, J. A. (1983) Effects of low-level ozone exposure on pulmonary function in adult and neonatal rats. In: Lee, S. D.; Mustafa, M. G.; Mehlman, M. A., eds. International symposium on the biomedical effects of ozone and related photochemical oxidants; March 1982; Pinehurst, NC Princeton, NJ: Princeton Scientific Publishers, Inc.; pp. 363-367. (Advances in modern environmental toxicology: v. 5).

Reasor, M. J.; Adams III, G. K.; Brooks, J. K.; Rubin, R. J. (1979) Enrichment of albumin and IgG in the airway secretions of dogs breathing ozone. J. Environ. Sci. Health C13: 335-346.

Reckner, L. R. (1974) Survey of users of EPA-Reference Method for measurement of non-methane hydrocarbons in ambient air. Research Triangle Park, NC: U.S. Environmental Protection Agency, EPA report no. EPA-650/4-75-008.

Regener, V. H. (1960) On a sensitive method for the recording of atmospheric ozone. JGR J. Geophys. Res. 65: 3975-3977.

Regener, V. H. (1964) Measurement of atmospheric ozone with the chemiluminescent method. JGR J. Geophys. Res. 69: 3795-3800.

Rehme, K. A.; Puzak, J. C.; Beard, M. E.; Smith, C. F.; Paur, R. J. (1981) Project summary: Evaluation of ozone calibration procedure. Research Triangle Park, NC: U.S. Environmental Protection Agency; EPA report no. EPA-600/S4-80-050.

Reinert, R. A.; Nelson, P. V. (1979) Sensitivity and growth of twelve elatior begonia cultivars to ozone. HortScience 14: 747-748.

Renzetti, N. A.; Bryan, R. J. (1961) Atmospheric sampling for aldehydes and eye irritation in Los Angeles smog - 1960. J. Air Pollut. Control Assoc. 11: 421-424.

Revis, N. W.; Major, T.; Dalbey, W. E. (1981) Cardiovascular effects of ozone and cadmium inhalation in the rat. In: Northrop Services, Inc., ed. Proceedings of the research planning workshop on health effects of oxidants; January 1980; Raleigh, NC. Research Triangle Park, NC: U.S. Environmental Protection Agency, Health Effects Research Laboratory; EPA-600/9-81-001; pp. 171-179. Available from: NTIS, Springfield, VA; PB81-178832.

Reynolds, R. W.; Chaffee, R. R. (1970) Studies on the combined effects of ozone and a hot environment on reaction time in subhuman primates. In: Project clean air: v. 2. Santa Barbara, CA: University of California; 8 pp; Research Project S-6.

Richter, H. G. (1983) Analysis of organic compound data gathered during 1980 in northeast corridor cities. Research Triangle Park, NC: U.S. Environmental Protection Agency; EPA report no. EPA-450/4-83-017.

Roehm, J. N.; Hadley, J. G.; Menzel, D. B. (1972) The influence of vitamin E on the lung fatty acids of rats exposed to ozone. Arch. Environ. Health 24: 237-242.

Roose, M. L.; Bradshaw, A. D.; Roberts, T. M. (1982) Evolution of resistance to gaseous air pollutants. In: Unsworth, M. H.; Ormrod, D. P., eds. Effects of gaseous air pollution in agriculture and horticulture. London: Butterworth Scientific; pp. 379-409.

Sabersky, R. H.; Sinema, D. A.; Shair, F. H. (1973) Concentrations, decay rates, and removal of ozone and their relation to establishing clean indoor air. Environ. Sci. Technol. 1: 347-353.

Salvin, V. S. (1969) Ozone fading of dyes. Text. Chem. Color. 1: 245-251.

Salvin, V. S.; Walker, R. A. (1955) Service fading of disperse dyestuffs by chemical agents other than the oxides of nitrogen. Text. Res. J. 24: 571-585.

Sato, S.; Kawakami, M.; Maeda, S.; Takishima, T. (1976a) Scanning electron microscopy of the lungs of vitamin E-deficient rats exposed to a low concentration of ozone. Am. Rev. Respir. Dis. 113: 809-821.

Sato, S.; Kawakami, M.; Maeda, S.; Takishima, T. (1976b) Electron microscopic studies on the effects of ozone on the lungs of vitamin E-deficient rats. Nippon Kyobu Shikkan Gakkai Zasshi 14: 355-365.

Sato, S.; Shimura, S.; Hirosa, T.; Maeda, S.; Kawakami, M.; Takishima, T.; Kimura, S. (1980) Effects of long-term ozone exposure and dietary vitamin E in rats. Tohoku J. Exp. Med. 130: 117-128.

Sato, S.; Shimura, S.; Kawakami, M.; Hirosa, T.; Maeda, S.; Takishima, T.; Kimura, S.; Yashiro, M.; Okazaki, S.; Ito, M. (1978) Biochemical and ultrastructural studies on the effects of long-term exposure of ozone on vitamin E-depleted rats. Nippon Kyobu Shikkan Gakkai Zasshi 16: 260-268.

Sawicki, E.; Hauser, T. R.; Stanley, T. W.; Elbert, W. (1961). The 3-methyl-2-benzothiazolone hydrazone test. Sensitive new methods for the detection, rapid estimation, and determination of aliphatic aldehydes. Anal. Chem. 33:93-96.

Scheutzle, D.; Rasmussen, R. A. (1978) The molecular composition of secondary aerosol particles formed from terpenes. J. Air Pollut. Control Assoc. 28: 236-240.

Schlipkoter, H.; Bruch, J. (1973) Functional and morphological alterations caused by exposure to ozone. Zentralbl. Bakteriol. Parasitenkd. Infektionskr. Hyg. Abt. 1: Orig. Reihe B 156: 486-499.

Schmitt, C. H. A. (1960) Lightfastness of dyestuffs on textiles. Am. Dyest. Rep. 49: 974-980.

Schmitt, C. H. A. (1962) Daylight fastness testing by the Langley System. Am. Dyest. Rep. 51: 664-675.

Schwartz, L. W.; Christman, C. A. (1979) Alveolar macrophage migration. Influence of lung lining material and acute lung insult. Am. Rev. Respir. Dis. 120: 429-439.

Schwartz, L. W.; Dungworth, D. L.; Mustafa, M. G.; Tarkington, B. K.; Tyler, W. S. (1976) Pulmonary responses of rats to ambient levels of ozone: effects of 7-day intermittent or continuous exposure. Lab. Invest. 34: 565-578.

Scott, D. B. M.; Lesher, E. C. (1963) Effect of ozone on survival and permeability of Escherichia coli. J. Bacteriol. 85: 567-576.

Seila, R. L. (1981) Nonurban hydrocarbon concentrations in ambient air north of Houston, TX. In: Bufalini, J. J.; Arnts, R. R., eds. Atmospheric Biogenic Hydrocarbons. Ann Arbor, MI: Ann Arbor Science Publishers, Inc.

Seiler, W.; Fishman, J. (1981) The distribution of carbon monoxide and ozone in the free troposphere. JGR J. Geophys. Res. 86: 7255-7265.

Sevcik, J. (1975) Detectors in Gas Chromatography. Amsterdam, The Netherlands: Elsevier Scientific Publishing Company.

Sexton, F. W.; McElroy, F. F.; Michie, R. M., Jr.; Thompson, V. L. (1981) A comparative evaluation of seven automatic ambient non-methane organic compound analyzers. Research Triangle Park, NC: U.S. Environmental Protection Agency; cited in: U.S. Environmental Protection Agency (1981), EPA report no. EPA-600/4-81-015.

Sexton, K.; Westberg, H. (1984) Nonmethane hydrocarbon composition of urban and rural atmospheres. Atmos. Environ. (in press).

Shannon, J. G.; Mulchi, C. L. (1974) Ozone damage to wheat varieties at anthesis. Crop Sci., 14: 335-337.

Sherwin, R. P.; Richters, V.; Okimoto, D. (1983) Type 2 pneumocyte hyperplasia in the lungs of mice exposed to an ambient level (O_3 ppm) of ozone. In: Lee, S. D.; Mustafa, M. G.; Mehlman, M. A., eds. International symposium on the biomedical effects of ozone and related photochemical oxidants; March 1982; Pinehurst, NC. Princeton, NJ: Princeton Scientific Publishers, Inc.; pp. 289-297. (Advances in modern environmental toxicology: v. 5).

Sielczak, M. W.; Denas, S. M.; Abraham, W. M. (1983) Airway cell changes in tracheal lavage of sheep after ozone exposure. J. Toxicol. Environ. Health 11: 545-553.

Silverman, F. (1979) Asthma and respiratory irritants (ozone). EHP Environ. Health Perspect. 29: 131-136.

Silverman, F.; Folinsbee, L. J.; Barnard, J.; Shephard, R. J. (1976) Pulmonary function changes in ozone - interaction of concentration and ventilation. J. Appl. Physiol. 41: 859-864.

Singh, H. B.; Salas, L. J. (1983a) Peroxyacetyl nitrate in the free troposphere. Nature (London) 302: 326-328.

Singh, H. B.; Salas, L. J. (1983b) Methodology for the analysis of peroxyacetyl nitrate (PAN) in the unpolluted atmosphere. Atmos. Environ. 17: 1507-1516.

Singh, H. B.; Salas, L. J.; Smith, A. J.; Shigeishi, H. (1981) Measurements of some potentially hazardous organic chemicals in urban atmospheres. Atmos. Environ. 15: 601-612.

Singh, H. B., Salas, L. J.; Stiles, R.; Shigeishi, H. (1982) Measurements of hazardous organic chemicals in the ambient atmosphere. Report on EPA Cooperative Agreement 805990. Research Triangle Park, NC: U.S. Environmental Protection Agency, Environmental Sciences Research Laboratory.

Smith, R. L. (1980) Ecology and field biology, 3rd ed. New York, NY: Harper and Row; pp. 11-199.

Smith, W. J. (1981) New York State Air Monitoring Data Report for the Northeast Corridor Regional Modeling Project. Albany, NY: New York State Department of Environment and Conservation.

Solic, J. J.; Hazucha, M. J.; Bromberg, P. A. (1982) Acute effects of 0.2 ppm ozone in patients with chronic obstructive pulmonary disease. Am. Rev. Respir. Dis. 125: 664-669.

Speit, G.; Vogel, W.; Wolf, M. (1982) Characterization of sister chromatid exchange induction by hydrogen peroxide. Environ. Mutagen. 4: 135-142.

Spicer, C. W.; Gemma, J. L; Joseph, D. W.; Sticksel, P. R.; Ward, G. F. (1976) The transport of oxidant beyond urban areas. Prepared for U.S. Environmental Protection Agency, Research Triangle Park, NC. Publication No. EPA-600/3-76-018.

Standing Air Monitoring Work Group. (1977) Air Monitoring Work Group. Air monitoring strategy for implementation plans. U.S. Environmental Protection Agency, Office of Air Quality Planning and Standards. Research Triangle Park, NC. June 1977.

Stark, R. W.; Cobb, F. W., Jr. (1969) Smog injury, root diseases and bark beetle damage in ponderosa pine. Calif. Agric. 23: 13-15.

Stephens, E. R. (1969) The formation, reactions, and properties of peroxyacyl nitrates (PANs) in photochemical air pollution. In: Pitts, J. N.; Metcalf, R. L., eds. Advances in environmental sciences and technology: vol. 1. New York, NY: Wiley-Interscience; pp. 119-146.

Stephens, E. R.; Burleson, F. R.; Cardiff, E. A. (1965) The production of pure peroxyacyl nitrates. J. Air Pollut. Control Assoc. 15: 87-89.

Stephens, E. R.; Price, M. A. (1973) Analysis of an important air pollutant --peroxyacetyl nitrate. J. Chem. Educ. 50: 351-354.

Stephens, R. J.; Buntman, D. J.; Negi, D. S.; Parkhurst, R. M.; Thomas, D. W. (1983) Tissue levels of vitamin E in the lung and the cellular response to injury resulting from oxidant gas exposure. Chest 83: 37S-39S.

Stephens, R. J.; Freeman, G.; Stara, J. F.; Coffin, D. L. (1973) Cytologic changes in dog lungs induced by chronic exposure to ozone. Am. J. Pathol. 73: 711-726.

Stephens, R. J.; Sloan, M. F.; Evans, M. J.; Freeman, G. (1974a) Early response of lung to low levels of ozone. Am. J. Pathol. 74: 31-58.

Stephens, R. J.; Sloan, M. F.; Evans, M. J.; Freeman, G. (1974b) Alveolar type 1 cell response to exposure to 0.5 ppm O_3 for short periods. Exp. Mol. Pathol. 20: 11-23.

Stephens, R. J.; Sloan, M. F.; Groth, D. G. (1976) Effects of long-term, low level exposure of NO_2 or O_3 on rat lungs. EHP Environ. Health Perspect. 16: 178-179.

Stephens, R. J.; Sloan, M. F.; Groth, D. G.; Negi, D. S.; Lunan, K. D. (1978) Cytologic responses of postnatal rat lungs to O_3 or NO_2 exposure. Am. J. Pathol. 93: 183-200.

Stevens, R. K.; Hodgeson, J. A. (1973) Application of chemiluminescent reactions to the measurement of air pollutants. Anal. Chem. 45: 443A-446A, 449A.

Stewart, R. M.; Weir, E. K.; Montgomery, M.R.; Niewoehner (1981) Hydrogen peroxide contracts airway smooth muscle: a possible endogenous mechanism. Respir. Physiol. 45: 333-342.

Stokinger, H. E.; Wagner, W. D.; Dobrogorski, O. J. (1957) Ozone toxicity studies, III. Chronic injury to lungs of animals following exposure at low level. AMA Arch. Ind. Health 16: 514-522.

Stokinger, H. E.; Wagner, W. D.; Wright, P. G. (1956) Studies on ozone toxicity. I. Potentiating effects of exercise and tolerance development. AMA Arch. Ind. Health 14: 158-162.

Taylor, O. C. (1969) Importance of peroxyacetyl nitrate (PAN) as a phytotoxic air pollutant. J. Air Pollut. Control Assoc. 19: 347-351.

Temple, P. J.; Taylor, O. C. (1983) World-wide ambient measurements of peroxyacetyl nitrate (PAN) and implications for plant injury. Atmos. Environ. 17: 1583-1587.

Tepper, J. L.; Weiss, B.; Cox, C. (1982) Microanalysis of ozone depression of motor activity. Toxicol. Appl. Pharmacol. 64: 317-326.

Tepper, J. L.; Weiss, B.; Wood, R. W. (1983) Behavioral indices of ozone exposure. In: Lee, S. D.; Mustafa, M. G.; Mehlman, M. A., eds. International symposium on the biomedical effects of ozone and related photochemical oxidants; March 1982; Pinehurst, NC. Princeton, NJ: Princeton Scientific Publishers, Inc.; pp. 515-526. (Advances in modern environmental toxicology: v. 5).

Thomas, G. B.; Fenters, J. D.; Ehrlich, R.; Gardner, D. E. (1981a) Effects of exposure to peroxyacetyl nitrate on susceptibility to acute and chronic bacterial infection. J. Toxicol. Environ. Health 8: 559-574.

Thomas, G. B.; Fenters, J. D.; Ehrlich, R.; Gardner, D. E. (1981b) Effects of exposure to ozone on susceptibility to experimental tuberculosis. Toxicol. Lett. 9: 11-17.

Thomas, G.; Fenters, J. D.; Ehrlich, R. (1979) Effect of exposure to PAN and ozone on susceptibility to chronic bacterial infection. Research Triangle Park, NC: U.S. Environmental Protection Agency, Health Effects Research Laboratory; EPA report no. EPA-600/1-79-001. Available from: NTIS, Springfield, VA; PB292267.

Thomas, M. D.; Hendericks, R. H.; Hill, G. R. (1950) Sulfur metabolism of plants. Effects of sulfur dioxide on vegetation. Industrial and Engineering Chemistry, 42: 2231-2235.

Thompson, C. R.; Hensel, E. G.; Kats, G. (1973) Outdoor-indoor levels of six air pollutants. J. Air Pollut. Control Assoc. 19: 347-351.

Thompson, C. R.; Kats, G.; Camerson, J. W. (1976) Effects of ambient photochemical oxidants on growth, yield, and ear characteristics of two sweet corn hybrids. J. Environ. Qual., 5: 410-412.

Tingey, D. T. (1977) Ozone induced alterations in plant growth and metabolism. In: Dimitriades, B., ed. International Conference on Photochemical Oxidant Pollution and its Control: Proceedings, Volume II, January 1977. EPA-600/3-77-001b. U.S. Environmental Protection Agency, Research Triangle Park, N.C. pp. 601-609

Tingey, D. T.; Heck, W. W.; Reinert, R. A. (1971) Effects of low concentrations of ozone and sulfur dioxide on foliage, growth and yield of radish. J. Am. Soc. Hort. Sci., 96: 369-371.

Tingey, D. T.; Reinert, R. A. (1975) The effects of ozone and sulfur dioxide singly and in combination on plant growth. Environ. Pollut., 9: 117-125.

Tingey, D. T.; Taylor, G. E. (1982) Variation in plant response to ozone: a conceptual model of physiological events. In: Unsworth, M. H.; Ormrod, D. P., eds. Effects of Gaseous Air Pollution in Agricultural and Horticulture. Butterworths, London. pp. 113-138

Tokiwa, Y.; Twiss, S.; deVera, E. A.; Mueller, P. K. (1972) Atmospheric ozone determination by amperometry and colorimetry. In: Mamantov, G.; Shults, W. D., eds. Determination of air quality. New York, NY: Plenum Publishing Co.; pp. 109-130.

Trams, E. G.; Lauter, C. J.; Brown, E. A. B.; Young, O. (1972) Cerebral cortical metabolism after chronic exposure to O_3. Arch. Environ. Health 24: 153-159.

Treshow, M.; Stewart, D. (1973) Ozone sensitivity of plants in natural communities. Biol. Conserv. 5: 205-214.

Tuazon, E. C.; Carter, W. P. L.; Winer, A. M.; Pitts, J. N., Jr. (1981) Reactions of hydrazines with ozone under simulated atmospheric conditions. Environ. Sci. Technol. 15: 823-828.

Tuazon, E. C.; Graham, R. A.; Winer, A. M.; Easton, R. R.; Pitts, J. N., Jr. Hanst, P. L. (1978) A kilometer pathlength Fourier-transform infrared system for the study of trace pollutants in ambient and synthetic atmospheres. Atmos. Environ. 12: 865-875.

Tuazon, E. C.; Winer, A. M.; Graham, R. A.; Pitts, J. N., Jr. (1981a) Atmospheric measurements of trace pollutants: long path Fourier transform infrared spectroscopy. Prepared for U.S. Environmental Protection Agency, Environmental Sciences Research Laboratory, Research Triangle Park, NC.

Tuazon, E. C.; Winer, A. M.; Pitts, J. N., Jr. (1981b) Trace pollutant concentrations in a multiday smog episode in the California South Coast Air Basin by long path length Fourier-transform infrared spectrometry. Environ. Sci. Technol. 15: 1232-1237.

Tyson, C. A.; Lunan, K. D.; Stephens, R. J. (1982) Age-related differences in GSH-shuttle enzymes in NO_2- or O_3-exposed rat lungs. Arch. Environ. Health 37: 167-176.

U.S. Congress. (1977) The Clean Air Act as Amended August 1977. P. L. 95-95. Washington, DC; U.S. Government Printing Office.

U.S. Department of Commerce, Bureau of the Census. (1982) Statistical Abstract of the United States, 1982-83. 103rd Ed. Washington, DC: U.S. Government Printing Office.

U.S. Department of Health, Education, and Welfare. (1970) Air quality criteria for photochemical oxidants. Washington, DC: National Air Pollution Control Administration; publication No. AP-63.

U.S. Environmental Protection Agency. (1982b). Air quality criteria for particulate matter and sulfur oxides. Research Triangle Park, NC: U.S. Environmental Protection Agency; EPA report no. EPA-600/8-82-029a,b,c,d.

U.S. Environmental Protection Agency. SAROAD data file for 1982. Office of Air Quality Planning and Standards, Research Triangle Park, NC 27711.

U.S. Environmental Protection Agency. SAROAD data file for 1976. Office of Air Quality Planning and Standards, Research Triangle Park, NC 27711.

U.S. Environmental Protection Agency. SAROAD data file for 1979. Office of Air Quality Planning and Standards, Research Triangle Park, NC 27711.

U.S. Environmental Protection Agency. SAROAD data file for 1980. Office of Air Quality Planning and Standards, Research Triangle Park, NC 27711.

U.S. Environmental Protection Agency. SAROAD data file for 1981. Office of Air Quality Planning and Standards, Research Triangle Park, NC 27711.

U.S. Environmental Protection Agency. (1971) Reference Methods. Code of Federal Regulations, Title 40, Part 50, Appendix D. Washington, DC: U.S. Government Printing Office.

U.S. Environmental Protection Agency. (1975) Ambient air monitoring reference and equivalent methods. Fed. Regist. 40: 7042-7070, February 18.

U.S. Environmental Protection Agency. (1976a). Ambient air monitoring reference and equivalent methods. Code of Federal Regulations, Title 40, Part 53.

U.S. Environmental Protection Agency. (1976b). Nitrogen dioxide measurement principle and calibration procedure. Notice of final rulemaking. Fed. Regist. 41:52686-5294, December 1.

U.S. Environmental Protection Agency. (1977) Quality assurance handbook for air pollution measurement systems. Research Triangle Park, NC: U.S. Environmental Protection Agency; EPA report no. EPA-600/4-77-027.

U.S. Environmental Protection Agency. (1978) Air quality criteria for ozone and other photochemical oxidants. Research Triangle Park, NC: U.S. Environmental Protection Agency; EPA report no. EPA-600/8-78-004.

U.S. Environmental Protection Agency. (1979a) Fed. Regist. 44(92): 27558, Thursday, May 10.

U.S. Environmental Protection Agency. (1979b) Fed. Regist. 44(219): 65069, Friday, November 9.

U.S. Environmental Protection Agency. (1979c) Fed. Regist. 44(242): 72589, Friday, December 14.

U.S. Environmental Protection Agency. (1979d) Calibration of ozone reference methods. Fed. Regist. 44: 8221-8233, February 8.

U.S. Environmental Protection Agency. (1980). Final emission inventory requirements for 1982 ozone state implementation plans. Research Triangle Park, NC: U.S. Environmental Protection Agency; EPA report no. EPA-450/4-80-016.

U.S. Environmental Protection Agency. (1981). Technical assistance document for the calibration and operation of automated ambient non-methane organic compound analyzers. Research Triangle Park, NC: U.S. Environmental Protection Agency, EPA report no. EPA-600/4-81-015.

U.S. Environmental Protection Agency. (1982a). Air quality criteria for oxides of nitrogen. Research Triangle Park, NC: U.S. Environmental Protection Agency; EPA report no. EPA-600/8-82-026.

Upham, J. B.; Haynie, F. H.; Spence, J. W. (1976) Fading of selected drapery fabrics by air pollutants. J. Air Pollut. Control Assoc. 26: 790-792.

Veith, A. G.; Evans, R. L. (1980) Effect of atmospheric pressure on ozone cracking of rubber. Polym. Testing 1: 27-38.

Veninga, T. S. (1967) Toxicity of ozone in comparison with ionizing radiation. Strahlentherapie 134: 469-477.

Veninga, T. S. (1970) Ozone-induced alterations in murine blood and liver. Presented at: Second international clean air congress; December; Washington, DC. Washington, DC: International Union of Air Pollution Prevention Associations; paper no. MB-15E.

Veninga, T. S.; Wagenaar, J.; Lemstra, W. (1981) Distinct enzymatic responses in mice exposed to a range of low doses of ozone. EHP Environ. Health Perspect. 39: 153-157.

Verweij, H.; Van Steveninck, J. (1980) Effects of semicarbazide on processes in human red blood cell membranes. Biochim. Biophys. Acta 602: 591-599.

Verweij, H.; Van Steveninck, J. (1981) Protective effects of semicarbazide and p-aminobenzoic acid against ozone toxicity. Biochim. Pharmacol. 30: 1033-1037.

Viezee, W.; Johnson, W. B.; Singh, H. B. (1979) Airborne measurements of stratospheric ozone intrusions into the troposphere over the United States. Final Report. SRI Project 6690 for Coordinating Research Council, Atlanta, Georgia.

Warshauer, D.; Goldstein, E.; Hoeprich, P. D.; Lippert, W. (1974) Effect of vitamin E and ozone on the pulmonary antibacterial defense mechanisms. J. Clin. Med. 83: 228-240.

Watanabe, S.; Frank, R.; Yokoyama, E. (1973) Acute effects of ozone on lungs of cats. I. Functional. Am. Rev. Respir. Dis. 108: 1141-1151.

Wayne, W. S.; Wehrle, P. F.; Carroll, R. E. (1967) Oxidant air pollution and athletic performance. J. Am. Med. Assoc. 199: 902-904.

Wegner, C. D. (1982) Characterization of dynamic respiratory mechanics by measurement of pulmonary and respiratory system impedance in adult bonnet monkeys (Macaca radiata): including the effects of long-term exposure to low-level ozone. Davis, CA: University of California; Ph.D. Dissertation.

Weiss, B.; Ferin, J.; Merigan, W.; Stern, S.; Cox, C. (1981) Modification of rat operant behavior by ozone exposure. Toxicol. Appl. Pharmacol. 58: 244-251.

Wenghoefer, H. M. (1974) Environmental effects on RFL adhesion. Rubber Chem. Technol. 47(5): 1066-1073.

Westberg, H. H.; Holdren, M. W.; Hill, H. H. (1980) Analytical methodology for the identification and quantification of vapor phase organic pollutants. CRC-APRAC Project No. CAPA-11-71, Coordinating Research Council, New York, NY.

Westberg, H.; Allwine, K.; Robinson, R. (1978) Measurement of light hydrocarbon and oxidant transport: Houston study, 1976. Research Triangle Park, NC: U.S. Environmental Protection Agency, Environmental Sciences Research Laboratory; EPA report no. EPA-600/3-78-662.

Westberg, H.; Lamb, B. (1982) Milwaukee ozone study - 1981. Final Report for Contract No. NRA 98571. Wisconsin Department of Natural Resources, Madison, WI.

Westberg, H.; Lamb, B. (1983) Ozone production and transport in the Atlanta, GA region. Final report for EPA grant no. CR 809221; Environmental Sciences Research Laboratory, U.S. Environmental Protection Agency; Research Triangle Park, NC.

Whittemore, A. S.; Korn, E. L. (1980) Asthma and air pollution in the Los Angeles area. Am. J. Public Health 70: 687-696.

Wilhour, R. G.; Neely, G. E. (1977) Growth response of conifers seedlings to low ozone concentrations. In: International Conference of Photochemical Oxidant Pollution and Its Control: Proceedings. Volume II. B. Dimitriades, ed. EPA-600/3-77-001b. U.S. Environmental Protection Agency, Research Triangle Park, N.C. pp. 635-645.

Williams, S. J.; Charles, J. M.; Menzel, D. B. (1980) Ozone-induced alterations in phenol red absorption from the rat lung. Toxicol. Lett. 6: 213-219.

Winer, A. M.; Peters, J. M.; Smith, J. P.; Pitts, J. N., Jr. (1974) Response of commercial chemiluminescent NO-NO_2 analysis to other nitrogen-containing compounds. Environ. Sci. Technol. 8:1118-1121.

Witz, G.; Amoruso, M. A.; Goldstein, B. D. (1983) Effect of ozone on alveolar macrophage function: membrane dynamic properties. In: Lee, S. D.; Mustafa, M. G.; Mehlman, M. A., eds. International symposium on the biomedical effects of ozone and related photochemical oxidants; March 1982; Pinehurst, NC. Princeton, NJ: Princeton Scientific Publishers, Inc.; pp. 263-272. (Advances in modern environmental toxicology: v. 5).

Woodwell, G. M. (1970) Effects of pollution on the structure and physiology of ecosystems. Science (Washington, D.C.) 168: 429-433.

Woodwell, G. M. (1974) Success, succession, and Adam Smith. BioScience 24: 81-87.

Xintaras, C.; Johnson, B. L.; Ulrich, C. E.; Terrill, R. E.; Sobecki, M. F. (1966) Application of the evoked response technique in air pollution toxicology. Toxicol. Appl. Pharmacol. 8: 77-87.

Yokoyama, E. (1969) A comparison of the effects of SO_2, NO_2 and O_3 on the pulmonary ventilation. Guinea pig exposure experiments. Sangyo Igaku 11: 563-568.

Yokoyama, E. (1974) On the maximal expiratory flow volume curve of rabbits exposed to ozone. Nipon Kyobu Shikkan Gakkai Zasshi 12: 556-561.

Yokoyama, E.; Frank, R. (1972) Respiratory uptake of ozone in dogs. Arch. Environ. Health 25: 132-138.

Zagraniski, R. T.; Leaderer, B. P.; Stolwijk, J. A. J. (1979) Ambient sulfates, photochemical oxidants, and acute health effects: an epidemiological study. Environ. Res. 19: 306-320.

Zaitsu, K.; Okhura, Y. (1980) New fluorogenic substrates for horseradish peroxidase: rapid and sensitive assays for hydrogen peroxide and peroxidase. Anal. Biochem. 109: 109-113.

Zelac, R. E.; Cromroy, H. L.; Bolch, Jr., W. E.; Dunavant, B. G.; Bevis, H. A. (1971a) Inhaled ozone as a mutagen. I. Chromosome aberrations induced in Chinese hamster lymphocytes. Environ. Res. 4: 262-282.

Zelac, R. E.; Cromroy, H. L.; Bolch, W. E., Jr.; Dunavant, B. G.; Bevis, H. A. (1971b) Inhaled ozone as a mutagen. II. Effect on the frequency of chromosome aberrations observed in irradiated Chinese hamsters. Environ. Res. 4: 325-342.

Zika, R. G.; Saltzman, E. S. (1982) Interaction of ozone and hydrogen peroxide in water: implications for analysis of H_2O_2 in air. Geophys. Res. Lett. 9: 231-234.

Zitnik, L. A.; Schwartz, L. W.; McQuillen, N. K.; Zee, Y. C.; Osebold, J. W. (1978) Pulmonary changes induced by low-level ozone: morphological observations. J. Environ. Pathol. Toxicol. 1: 365-376.